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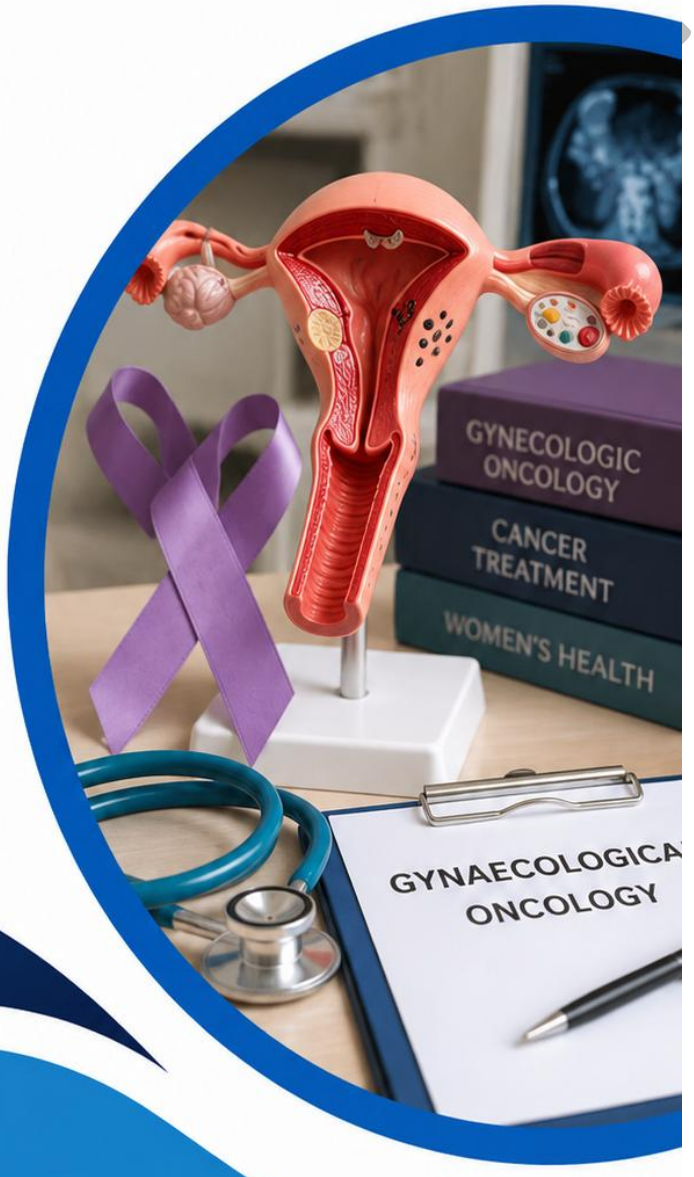
OBG 506

GYNAECOLOGICAL ONCOLOGY



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Course code: OBG 506

Course title: Gynaecological Oncology

Course credit load: 1 Unit

Series 1: Vulval and Vaginal Lesions

- **Part 1.1: Vulval Anatomy and Benign and Pre-malignant Lesions**
    - Sub Part 1.1.1: Anatomy of the vulva, femoral triangle, and lower abdominal wall
    - Sub Part 1.1.2: Benign lesions of the vulva
    - Sub Part 1.1.3: Pre-malignant lesions of the vulva and pruritus vulvae
- **Part 1.2: Malignant Lesions of the Vulva**
    - Sub Part 1.2.1: Epidemiology and aetiology of vulval cancer
    - Sub Part 1.2.2: Histopathology and clinical presentation of vulval cancer
    - Sub Part 1.2.3: Principles of treatment of vulval cancer
- **Part 1.3: Diseases of the Vagina**
    - Sub Part 1.3.1: Vaginal discharge and benign lesions of the vagina
    - Sub Part 1.3.2: Pre-malignant lesions of the vagina
    - Sub Part 1.3.3: Malignant lesions of the vagina

Introduction

Picture a woman referred to a gynaecological oncology clinic with a persistent vulval lesion she has been quietly worried about for months. Whether her diagnosis turns out to be entirely benign, a pre-malignant condition requiring surveillance, or something more serious, your ability to recognise, investigate, and explain it begins with a solid grasp of vulval and vaginal anatomy and pathology. This Series lays that essential foundation for the whole of this course on gynaecological oncology, before we turn in later Series to the cervix, uterus, ovary, and the specific therapies used to treat gynaecological cancer.

The aim of this Series is to equip you with a thorough understanding of vulval anatomy, the benign, pre-malignant, and malignant lesions of the vulva, and the diseases of the vagina.

We shall commence this Series by examining vulval anatomy and its benign and pre-malignant lesions. Next, we will consider malignant lesions of the vulva, including vulval cancer

epidemiology, histopathology, and treatment. Finally, we will conclude by examining diseases of the vagina, from benign discharge through to pre-malignant and malignant lesions.

Series Learning Outcomes

Upon completing this Series, you should be able to:

- **SLO 1.1:** describe the anatomy of the vulva, femoral triangle, vaginal region, and lower abdominal wall, including blood supply, nerve distribution, and lymph drainage,
- **SLO 1.2:** describe benign and pre-malignant lesions of the vulva, including pruritus vulvae,
- **SLO 1.3:** illustrate the epidemiology and aetiology of vulval cancer,
- **SLO 1.4:** identify the histopathology and list the principles of treatment of vulval cancer,
- **SLO 1.5:** describe benign and pre-malignant lesions of the vagina, and
- **SLO 1.6:** describe malignant lesions of the vagina.

1.1 Vulval Anatomy and Benign and Pre-malignant Lesions

1.1.1 Anatomy of the vulva, femoral triangle, and lower abdominal wall

The vulva comprises the mons pubis, labia majora and minora, clitoris, vestibule, and Bartholin's and Skene's glands, with blood supply principally from the internal and external pudendal arteries, branches of the internal iliac and femoral arteries respectively, and sensory innervation from the pudendal nerve alongside contributions from the ilioinguinal and genitofemoral nerves.

Lymphatic drainage of the vulva is of particular clinical importance given its direct relevance to the staging and surgical management of vulval cancer, draining principally to the superficial inguinal lymph nodes within the femoral triangle, then to the deep inguinal and femoral nodes, and subsequently to the external iliac and pelvic nodes, with the femoral triangle itself bordered by the inguinal ligament, sartorius muscle, and adductor longus muscle, and containing the femoral artery, vein, and nerve alongside these superficial inguinal nodes.

Fill in the blank: Sensory innervation of the vulva arises principally from the _____ nerve, alongside contributions from the ilioinguinal and genitofemoral nerves. Lymphatic drainage of the vulva passes principally to the superficial inguinal lymph nodes within the femoral _____.

1.1.2 Benign lesions of the vulva

Benign vulval lesions include Bartholin's cyst (accumulation of secretions within an obstructed gland duct), sebaceous cysts, vulval varicosities (particularly common in pregnancy given increased pelvic venous pressure), and vulval dermatoses such as lichen sclerosus (a chronic inflammatory condition causing thinning, whitening, and scarring of the vulval skin) and lichen simplex chronicus (thickened skin from chronic scratching), each requiring careful clinical assessment and, where the diagnosis remains uncertain, biopsy.

Lichen sclerosus carries a small but genuinely important increased risk of subsequent vulval squamous cell carcinoma, meaning any woman with this diagnosis warrants regular follow-up and a low threshold for biopsy of any new, persistent, or atypical-appearing area, distinguishing this specific benign dermatosis from most other benign vulval conditions, which do not carry a comparable malignant potential.

Fill in the blank: Lichen sclerosus is a chronic inflammatory condition causing thinning, whitening, and _____ of the vulval skin. Lichen sclerosus carries a small but genuinely important increased risk of subsequent vulval squamous cell _____.

1.1.3 Pre-malignant lesions of the vulva and pruritus vulvae

Vulval intraepithelial neoplasia (VIN) is the pre-malignant precursor to vulval squamous cell carcinoma, classified into a usual type (strongly associated with persistent high-risk human papillomavirus infection, typically affecting younger women) and a differentiated type (associated with lichen sclerosus and typically affecting older women), each with a somewhat different natural history and risk of progression to invasive malignancy if left untreated.

Pruritus vulvae (vulval itching) is a common, non-specific symptom with a broad differential diagnosis, including infective causes (candidiasis, other infections), dermatological conditions (lichen sclerosus, lichen simplex chronicus, contact dermatitis), and, less commonly, VIN or invasive malignancy itself, meaning any woman with persistent, unexplained pruritus vulvae warrants careful examination and, where clinically indicated, biopsy of any visible abnormality rather than reflexive symptomatic treatment alone.

Fill in the blank: Vulval intraepithelial neoplasia is classified into a usual type associated with high-risk human _____ infection, and a differentiated type associated with lichen sclerosus. Persistent, unexplained pruritus vulvae warrants careful examination and, where indicated, _____ of any visible abnormality.

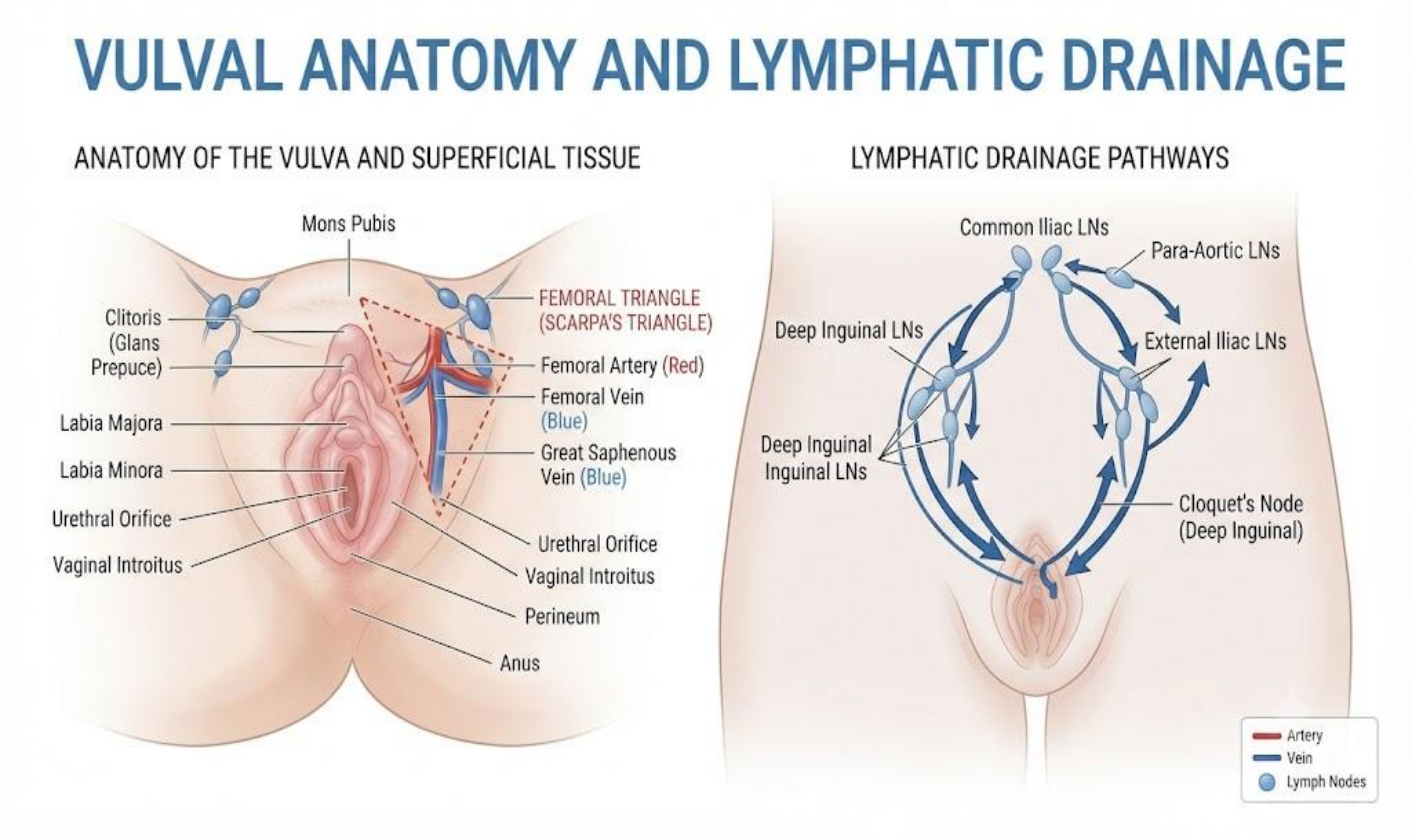

Figure 1.1: Vulval anatomy, the femoral triangle, and lymphatic drainage pathway.

Pilot questions 1.1

1. Describe the anatomical structures comprising the vulva and their blood supply and innervation. (Linked to SLO 1.1)
2. Describe the lymphatic drainage of the vulva and its clinical relevance. (Linked to SLO 1.1)
3. Describe the common benign lesions of the vulva. (Linked to SLO 1.2)
4. Explain the malignant potential of lichen sclerosus. (Linked to SLO 1.2)
5. Describe vulval intraepithelial neoplasia and its two classified types. (Linked to SLO 1.2)

1.2 Malignant Lesions of the Vulva

1.2.1 Epidemiology and aetiology of vulval cancer

Vulval cancer is a relatively uncommon gynaecological malignancy, predominantly affecting older, postmenopausal women, though a genuinely significant minority of cases occur in younger

women, typically associated with persistent high-risk human papillomavirus infection and usual-type vulval intraepithelial neoplasia rather than the lichen sclerosus-associated pathway more typical of older women.

Recognised risk factors for vulval cancer include persistent high-risk HPV infection, smoking (which acts synergistically with HPV to increase risk), immunosuppression, a history of lichen sclerosus, and a previous history of cervical or vaginal intraepithelial neoplasia or cancer, reflecting the broadly shared aetiological pathway of persistent HPV infection across much of the lower genital tract.

Fill in the blank: Vulval cancer predominantly affects older, postmenopausal women, though a significant minority of cases occur in _____ women. Smoking acts synergistically with _____ infection to increase the risk of vulval cancer.

1.2.2 Histopathology and clinical presentation of vulval cancer

Squamous cell carcinoma accounts for the great majority of vulval cancers, arising either from HPV-associated usual-type VIN or from lichen sclerosus-associated differentiated VIN, with less common histological subtypes including melanoma, Bartholin's gland carcinoma, and basal cell carcinoma, each carrying somewhat different clinical behaviour and prognosis.

Vulval cancer typically presents with a persistent vulval lump, ulcer, or area of skin change, frequently accompanied by pruritus, bleeding, or pain, though presentation can be genuinely non-specific, and delayed presentation, sometimes reflecting embarrassment or reluctance to seek attention for a genital symptom, remains a recognised, important contributor to more advanced disease at diagnosis in some women.

Fill in the blank: Squamous cell carcinoma accounts for the great majority of vulval cancers, arising from either usual-type or _____-associated differentiated VIN. Delayed presentation of vulval cancer remains a recognised, important contributor to more advanced _____ at diagnosis.

1.2.3 Principles of treatment of vulval cancer

Surgical management is the primary treatment for early-stage vulval cancer, with wide local excision, achieving an adequate margin of normal tissue around the tumour, together with assessment of inguinofemoral lymph nodes, either by sentinel lymph node biopsy in appropriately selected early-stage disease or formal inguinofemoral lymphadenectomy, given the direct relevance of nodal status to both prognosis and further adjuvant treatment decisions.

Radiotherapy and chemoradiotherapy are used for more advanced disease, where surgery alone would be unlikely to achieve adequate margins or would result in unacceptable functional or cosmetic consequences, or as adjuvant treatment following surgery where high-risk pathological features, such as involved margins or positive lymph nodes, are identified, with the specific treatment approach genuinely individualised according to disease stage, extent, and the woman's own overall clinical circumstances.

Fill in the blank: Surgical management of vulval cancer includes wide local excision and assessment of _____ lymph nodes. Radiotherapy is used for more advanced disease or as _____ treatment following surgery when high-risk features are identified.

Category	Details
Risk Factors	HPV infection, smoking, chronic vulval dermatoses (lichen sclerosus), immunosuppression, older age
Histology	Squamous cell carcinoma (most common), melanoma, adenocarcinoma, basal cell carcinoma, sarcoma
Presentation	Vulval lump or ulcer, pruritus, pain, bleeding, non-healing lesion, inguinal lymphadenopathy
Treatment Principles	Wide local excision or radical vulvectomy depending on stage; inguinal lymph node dissection; radiotherapy for advanced disease; chemotherapy in selected cases; multidisciplinary approach

Table 1.2: Vulval cancer risk factors, histology, presentation, and treatment principles.

Pilot questions 1.2

1. Describe the epidemiology of vulval cancer. (Linked to SLO 1.3)
2. List the risk factors for vulval cancer. (Linked to SLO 1.3)
3. Describe the predominant histological subtype of vulval cancer and its two developmental pathways. (Linked to SLO 1.4)
4. Describe the typical clinical presentation of vulval cancer. (Linked to SLO 1.4)
5. List the principles of treatment of vulval cancer. (Linked to SLO 1.4)

1.3 Diseases of the Vagina

1.3.1 Vaginal discharge and benign lesions of the vagina

Vaginal discharge is a common presenting symptom with a wide differential, from physiological discharge to pathological discharge from infection such as bacterial vaginosis, candidiasis, or trichomoniasis, discussed in greater depth elsewhere in this broader curriculum, with persistent, unexplained, or bloodstained discharge, particularly in an older woman, warranting careful examination to exclude a structural or malignant cause.

Benign lesions of the vagina include vaginal cysts (such as a Gartner's duct cyst, a remnant of the mesonephric duct, typically found on the lateral vaginal wall), vaginal polyps, and, less commonly, vaginal endometriosis, each generally identified incidentally or presenting with discomfort, dyspareunia, or a palpable lump, and generally managed conservatively unless symptomatic or diagnostically uncertain.

Fill in the blank: Persistent, unexplained, or bloodstained vaginal discharge, particularly in an older woman, warrants careful examination to exclude a structural or _____ cause. A Gartner's duct cyst is a remnant of the _____ duct, typically found on the lateral vaginal wall.

1.3.2 Pre-malignant lesions of the vagina

Vaginal intraepithelial neoplasia (VAIN) is the pre-malignant precursor to vaginal squamous cell carcinoma, strongly associated with persistent high-risk human papillomavirus infection and frequently identified in a woman with a coexisting or previous history of cervical intraepithelial neoplasia or cervical cancer, reflecting the shared field effect of HPV infection across the lower genital tract.

VAIN is often identified incidentally during colposcopic assessment for an abnormal cervical screening result, or during surveillance following previous treatment for cervical intraepithelial neoplasia, given the recognised, elevated risk of VAIN in this specific population, with management ranging from surveillance for low-grade disease to laser ablation, excision, or, for extensive disease, topical treatment for confirmed high-grade VAIN.

Fill in the blank: Vaginal intraepithelial neoplasia is strongly associated with persistent high-risk human _____ infection. VAIN is often identified incidentally during colposcopic assessment or during surveillance following previous treatment for cervical intraepithelial _____.

1.3.3 Malignant lesions of the vagina

Primary vaginal cancer is a genuinely rare gynaecological malignancy, with squamous cell carcinoma the most common histological subtype, sharing a broadly similar aetiological pathway to cervical and vulval cancer through persistent high-risk HPV infection, and typically presenting with abnormal vaginal bleeding, discharge, or a palpable mass, most commonly in older women.

Given its rarity any tumour apparently arising in the vagina must be carefully assessed to exclude direct extension or metastasis from an adjacent primary malignancy, particularly cervical or vulval cancer, before a genuine primary vaginal cancer diagnosis is confirmed, with treatment

principles broadly following those established for cervical cancer, typically combining surgery, radiotherapy, or chemoradiotherapy according to disease stage and extent.

Fill in the blank: Squamous cell carcinoma is the most common histological subtype of primary vaginal cancer, sharing a broadly similar aetiological pathway through persistent high-risk _____ infection. Any tumour apparently arising in the vagina must be assessed to exclude direct extension or _____ from an adjacent primary malignancy.

Category	Key Features and Management
Benign Lesions	Vaginitis (infective, atrophic, allergic); vaginal cysts; Gartner's duct cyst; leiomyoma. Management: treat underlying cause, antibiotics/antifungals, excision if symptomatic.
Pre-malignant Lesions	Vaginal intraepithelial neoplasia (VAIN), often HPV-related. Features: abnormal cytology, colposcopic changes. Management: local excision, laser ablation, topical agents (imiquimod).
Malignant Lesions	Squamous cell carcinoma (most common), adenocarcinoma, melanoma, sarcoma. Features: vaginal bleeding, discharge, mass, pain. Management: surgery (wide excision, vaginectomy), radiotherapy, chemotherapy depending on stage.

Box 1.3: Benign, pre-malignant, and malignant lesions of the vagina.

Pilot questions 1.3

1. Describe the causes of vaginal discharge and when further investigation is warranted. (Linked to SLO 1.5)
2. Describe the common benign lesions of the vagina. (Linked to SLO 1.5)
3. Describe vaginal intraepithelial neoplasia and its association with cervical disease. (Linked to SLO 1.5)
4. Describe the epidemiology and presentation of primary vaginal cancer. (Linked to SLO 1.6)
5. Explain why apparent vaginal malignancy must be assessed to exclude an adjacent primary tumour. (Linked to SLO 1.6)

Series Summary

This Series has covered vulval anatomy and its benign and pre-malignant lesions, followed by malignant lesions of the vulva, including vulval cancer epidemiology, histopathology, and

treatment. It concluded with diseases of the vagina, from benign discharge through to pre-malignant and malignant lesions.

You should now be able to describe vulval anatomy and lymphatic drainage, describe benign and pre-malignant vulval lesions, illustrate the epidemiology and aetiology of vulval cancer, identify its histopathology and treatment principles, and describe benign, pre-malignant, and malignant lesions of the vagina (Linked to SLOs 1.1 to 1.6).

Glossary of Terms

- **Bartholin's cyst:** accumulation of secretions within an obstructed Bartholin's gland duct.
- **Femoral triangle:** an anatomical region bordered by the inguinal ligament, sartorius, and adductor longus, containing the superficial inguinal lymph nodes.
- **Gartner's duct cyst:** a benign vaginal cyst arising as a remnant of the mesonephric duct, typically on the lateral vaginal wall.
- **Lichen sclerosus:** a chronic inflammatory condition causing thinning, whitening, and scarring of the vulval skin, with a small malignant potential.
- **Pruritus vulvae:** vulval itching, a common, non-specific symptom with a broad differential diagnosis.
- **Sentinel lymph node biopsy:** a technique identifying and sampling the first lymph node draining a tumour, used in selected early vulval cancer.
- **Vaginal intraepithelial neoplasia (VAIN):** the pre-malignant precursor to vaginal squamous cell carcinoma, associated with high-risk HPV infection.
- **Vulval intraepithelial neoplasia (VIN):** the pre-malignant precursor to vulval squamous cell carcinoma, classified as usual or differentiated type.
- **Wide local excision:** surgical removal of a tumour with an adequate margin of surrounding normal tissue.
- **Inguinofemoral lymphadenectomy:** surgical removal of the inguinal and femoral lymph nodes, performed in vulval cancer staging and treatment.
- **Pudendal nerve:** the principal sensory nerve of the vulva and perineum.
- **Differentiated VIN:** a subtype of vulval intraepithelial neoplasia associated with lichen sclerosus, typically affecting older women.

Concept Check Questions [Series 1]

Objective questions

1. Sensory innervation of the vulva arises principally from the _____ nerve.
2. Lichen sclerosus carries a small but important increased risk of subsequent vulval squamous cell _____.
3. Smoking acts synergistically with _____ infection to increase the risk of vulval cancer.
4. A Gartner's duct cyst is a remnant of the _____ duct, typically found on the lateral vaginal wall.
5. VAIN is often identified incidentally during colposcopic assessment or during surveillance following treatment for cervical intraepithelial _____.

Short-answer questions

6. Describe the lymphatic drainage of the vulva and its clinical relevance. (Linked to SLO 1.1)
7. Explain the malignant potential of lichen sclerosus. (Linked to SLO 1.2)
8. Describe the typical clinical presentation of vulval cancer. (Linked to SLO 1.4)
9. Describe vaginal intraepithelial neoplasia and its association with cervical disease. (Linked to SLO 1.5)
10. Explain why apparent vaginal malignancy must be assessed to exclude an adjacent primary tumour. (Linked to SLO 1.6)

Long-answer questions

11. Describe the anatomy of the vulva and its benign and pre-malignant lesions. (Linked to SLO 1.1, SLO 1.2)
12. Describe the epidemiology, aetiology, and histopathology of vulval cancer. (Linked to SLO 1.3, SLO 1.4)
13. List the principles of treatment of vulval cancer. (Linked to SLO 1.4)
14. Describe the benign and pre-malignant lesions of the vagina. (Linked to SLO 1.5)
15. Describe the epidemiology, presentation, and diagnostic considerations of malignant vaginal lesions. (Linked to SLO 1.6)

Answers to Concept Check Questions [Series 1]

Objective questions

1. Pudendal.
2. Carcinoma.
3. HPV.
4. Mesonephric.
5. Neoplasia.

Short-answer questions

6. It drains principally to the superficial inguinal lymph nodes within the femoral triangle, directly relevant to cancer staging and surgery.
7. It carries a small but important increased risk of subsequent vulval squamous cell carcinoma, warranting regular follow-up.
8. A persistent vulval lump, ulcer, or area of skin change, often with pruritus, bleeding, or pain.
9. VAIN is associated with high-risk HPV and frequently coexists with or follows cervical intraepithelial neoplasia or cancer.
10. Vaginal cancer is rare, so extension or metastasis from an adjacent cervical or vulval primary must be excluded first.

Long-answer questions

11. **Basic response:** The vulva comprises several structures with pudendal innervation and inguinal lymphatic drainage, with benign lesions including cysts, varicosities, and dermatoses such as lichen sclerosus.

Value-added response: Lichen sclerosus and VIN both carry malignant potential, meaning any persistent or atypical vulval lesion warrants a low threshold for biopsy.

12. **Basic response:** Vulval cancer predominantly affects older women through HPV or lichen sclerosus pathways, with squamous cell carcinoma the predominant histology.

Value-added response: Delayed presentation, often from embarrassment, contributes to more advanced disease at diagnosis in some women.

13. **Basic response:** Treatment combines wide local excision with inguinofemoral lymph node assessment, escalating to radiotherapy for advanced disease or high-risk pathological features.

Value-added response: Treatment approach is genuinely individualised according to disease stage, extent, and the woman's overall clinical circumstances.

14. **Basic response:** Vaginal lesions range from benign discharge and cysts through VAIN to rare primary vaginal cancer, each sharing considerable overlap with cervical and vulval disease.

Value-added response: VAIN reflects the shared field effect of HPV across the lower genital tract, often coexisting with cervical disease.

15. **Basic response:** Primary vaginal cancer is rare, predominantly squamous cell carcinoma, and any apparent case must exclude an adjacent primary tumour first.

Value-added response: Treatment principles for vaginal cancer broadly follow those for cervical cancer, combining surgery, radiotherapy, or chemoradiotherapy.

Answers to Pilot Questions [Series 1]

Part 1.1

1. Mons pubis, labia majora and minora, clitoris, vestibule, and Bartholin's and Skene's glands, with pudendal artery blood supply and pudendal nerve innervation.
2. Drains principally to superficial inguinal nodes, then deep inguinal, femoral, and pelvic nodes, directly relevant to cancer staging.
3. Bartholin's cyst, sebaceous cysts, vulval varicosities, and dermatoses including lichen sclerosus and lichen simplex chronicus.
4. It carries a small but important increased risk of subsequent vulval squamous cell carcinoma.
5. Usual type, associated with high-risk HPV and younger women, and differentiated type, associated with lichen sclerosus and older women.

Part 1.2

1. A relatively uncommon malignancy predominantly affecting older, postmenopausal women, with a minority in younger women via HPV.

2. Persistent high-risk HPV, smoking, immunosuppression, lichen sclerosus, and previous cervical or vaginal neoplasia.
3. Squamous cell carcinoma, arising from HPV-associated usual-type VIN or lichen sclerosus-associated differentiated VIN.
4. A persistent vulval lump, ulcer, or skin change, often with pruritus, bleeding, or pain.
5. Wide local excision with inguinofemoral lymph node assessment, escalating to radiotherapy or chemoradiotherapy for advanced disease.

Part 1.3

1. Persistent, unexplained, or bloodstained discharge, particularly in an older woman, warrants examination to exclude structural or malignant cause.
2. Gartner's duct cyst, vaginal polyps, and vaginal endometriosis, generally managed conservatively unless symptomatic.
3. VAIN is the pre-malignant precursor to vaginal cancer, strongly associated with HPV and often coexisting with cervical disease.
4. A rare malignancy, predominantly squamous cell carcinoma, typically presenting with bleeding, discharge, or a mass in older women.
5. Vaginal cancer is rare, so direct extension or metastasis from an adjacent cervical or vulval primary must first be excluded.

References and Attributions [Series 1]

Textual References

- Hoffman, B. L., Schorge, J. O., Halvorson, L. M. et al. (2020). Williams Gynecology (4th ed.). McGraw Hill.
- Berek, J. S. and Berek, D. L. (2019). Berek and Novak's Gynecology (16th ed.). Wolters Kluwer.
- International Federation of Gynecology and Obstetrics (2021). FIGO Cancer Report. FIGO.
- Royal College of Obstetricians and Gynaecologists (2014). Green-top Guideline No. 58: Vulval Cancer. RCOG Press.

Figures, Plates, Tables, and Boxes

- Figure 1.1: Vulval anatomy, the femoral triangle, and lymphatic drainage pathway. AI-generated using the prompt: "Create a professional medical diagram titled Vulval Anatomy and Lymphatic Drainage, showing labelled structures, the femoral triangle, and lymphatic drainage pathway. Clean clinical educational diagram style."
- Table 1.2: Vulval cancer risk factors, histology, presentation, and treatment principles. AI-generated using the prompt: "Create a clean reference table titled Vulval Cancer Overview, listing risk factors, histology, presentation, and treatment. Simple clinical reference table style with outside border."
- Box 1.3: Benign, pre-malignant, and malignant lesions of the vagina. AI-generated using the prompt: "Create a simple single-column reference box with an outside border titled Diseases of the Vagina, listing benign, pre-malignant, and malignant lesions with key features. Clinical reference box style."

Series 2: Cervical Disorders and Cancer

- **Part 2.1: Disorders of the Cervix and Precursors to Cancer**
    - Sub Part 2.1.1: Benign lesions of the cervix
    - Sub Part 2.1.2: Pre-malignant lesions of the cervix and natural history
    - Sub Part 2.1.3: Cervical cancer incidence and risk factors
- **Part 2.2: Cervical Cancer: Presentation, Diagnosis, and Staging**
    - Sub Part 2.2.1: Epidemiology, aetiology, and clinical presentation
    - Sub Part 2.2.2: Examination under anaesthesia, biopsy, and diagnostic workup
    - Sub Part 2.2.3: Staging of cervical cancer
- **Part 2.3: Cervical Cancer: Treatment, Prognosis, and Prevention**
    - Sub Part 2.3.1: Treatment modalities in cervical cancer
    - Sub Part 2.3.2: Palliative care and prognosis
    - Sub Part 2.3.3: Prevention of cervical cancer

Introduction

In the last Series, we explored vulval and vaginal lesions. We now turn to the cervix, the site of one of the most common gynaecological malignancies worldwide and in Nigeria specifically, and, remarkably, one of the most genuinely preventable cancers in the whole of medicine. From benign polyps through the pre-malignant CIN spectrum to invasive cervical cancer itself, this Series builds the knowledge you need to recognise, stage, treat, and, most importantly, help prevent this disease.

The aim of this Series is to equip you with a thorough understanding of benign and pre-malignant disorders of the cervix, and the epidemiology, diagnosis, staging, treatment, and prevention of cervical cancer.

We shall commence this Series by examining disorders of the cervix and the precursors to cervical cancer, including cervical intraepithelial neoplasia. Next, we will consider cervical cancer presentation, diagnosis, and staging. Finally, we will conclude by examining cervical cancer treatment, palliative care, prognosis, and prevention.

Series Learning Outcomes

Upon completing this Series, you should be able to:

- **SLO 2.1:** describe benign lesions of the cervix,
- **SLO 2.2:** enumerate cervical cancer incidence, precursors, natural history, and risk factors,
- **SLO 2.3:** explain the epidemiology, aetiology, and presentation of cervical cancer,
- **SLO 2.4:** discuss how to conduct examination under anaesthesia, biopsy, and staging,
- **SLO 2.5:** list the staging of cervical cancer,
- **SLO 2.6:** list the treatment modalities in cervical cancer, and
- **SLO 2.7:** describe palliative care, prognosis, and prevention of cervical cancer.

2.1 Disorders of the Cervix and Precursors to Cancer

2.1.1 Benign lesions of the cervix

Cervical polyps are the most common benign cervical lesion, arising from the endocervical canal, typically presenting incidentally or with intermenstrual or post-coital bleeding, generally managed by simple avulsion in the outpatient clinic, with histological examination of the excised polyp routinely performed to exclude the rare possibility of underlying malignant change.

Cervical ectropion (eversion of the columnar epithelium of the endocervical canal onto the visible surface of the cervix, common in younger women, pregnancy, and with combined hormonal contraceptive use) is an entirely physiological finding, generally asymptomatic but occasionally causing increased discharge or post-coital bleeding, and, once malignancy has been appropriately excluded through routine cervical screening, does not itself require specific treatment unless genuinely symptomatic.

Fill in the blank: Cervical polyps are generally managed by simple _____ in the outpatient clinic. Cervical ectropion is common in younger women, pregnancy, and with combined hormonal _____ use.

2.1.2 Pre-malignant lesions of the cervix and natural history

Cervical intraepithelial neoplasia (CIN) is the pre-malignant precursor to cervical squamous cell carcinoma, classified by the depth of epithelial involvement as CIN 1 (low-grade, confined to the lower third of the epithelium), CIN 2 (moderate-grade, extending into the middle third),

and CIN 3 (high-grade, extending into the full thickness of the epithelium), with each grade carrying a progressively greater risk of progression to invasive cancer if left untreated.

The natural history of CIN is genuinely variable: low-grade CIN 1 frequently regresses spontaneously, particularly in younger women, without any specific treatment, while high-grade CIN 2 and CIN 3 carry a substantially greater risk of persistence or progression to invasive cancer over subsequent years if left untreated, a distinction of considerable practical importance directly guiding whether surveillance or active treatment is the more appropriate management approach for an individual woman.

Fill in the blank: CIN is classified by depth of epithelial involvement into CIN 1, CIN 2, and CIN _____. Low-grade CIN 1 frequently _____ spontaneously, particularly in younger women, without specific treatment.

2.1.3 Cervical cancer incidence and risk factors

Cervical cancer remains one of the most common gynaecological malignancies globally and in Nigeria specifically, with incidence disproportionately concentrated in low- and middle-income countries where organised cervical screening programmes are less consistently established, reflecting the genuinely preventable nature of the great majority of cervical cancer cases through timely detection and treatment of its pre-malignant precursors.

Persistent infection with high-risk human papillomavirus (particularly types 16 and 18, together accounting for the majority of cases) is established as the necessary underlying cause of cervical cancer, with additional recognised risk factors including early age at first intercourse, multiple sexual partners, smoking, immunosuppression (including HIV infection), and lack of engagement with cervical screening, each independently increasing the risk of progression from persistent HPV infection to invasive malignancy.

Fill in the blank: Persistent infection with high-risk _____ is established as the necessary underlying cause of cervical cancer. HPV types 16 and _____ together account for the majority of cervical cancer cases.

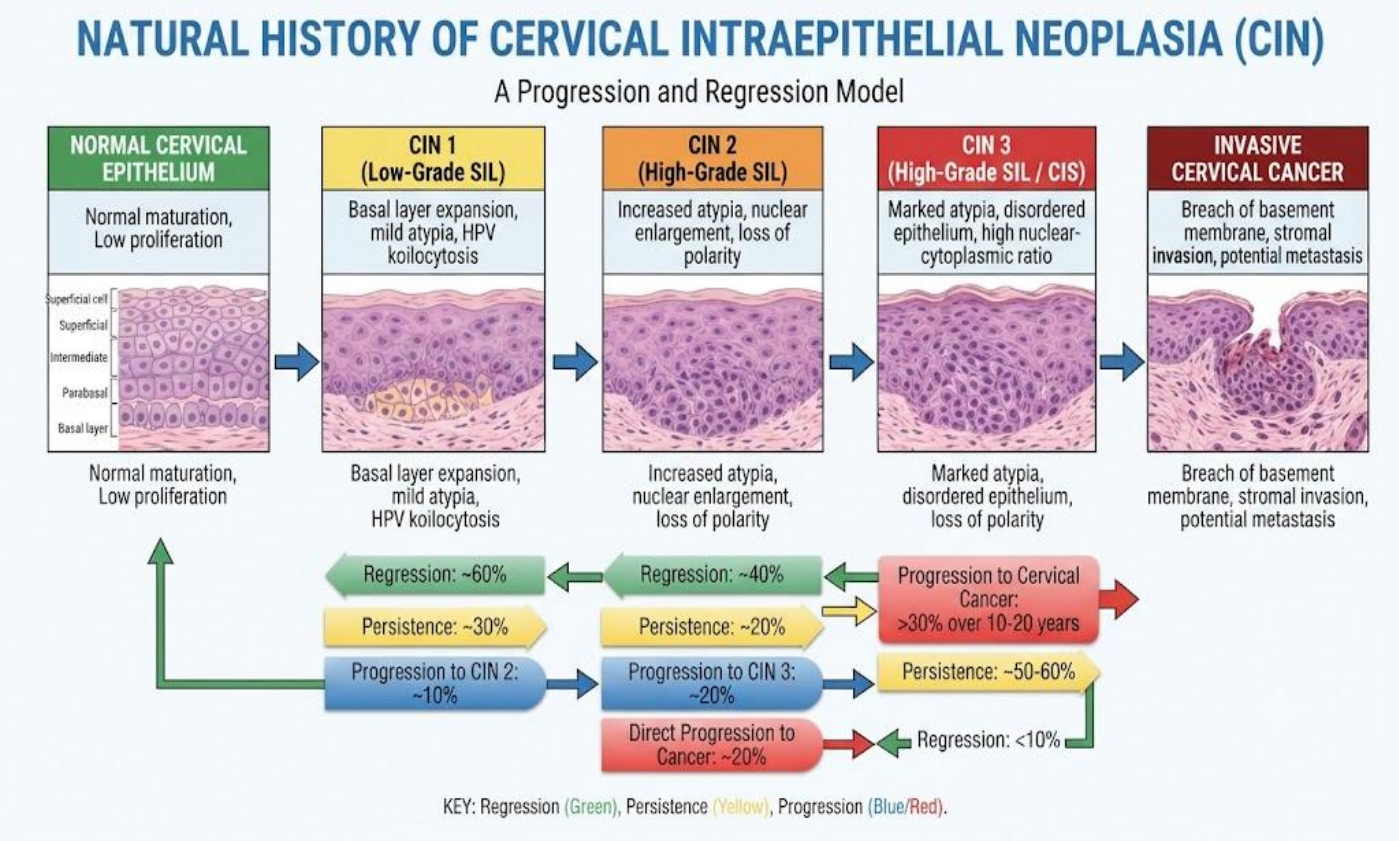

Figure 2.1: Natural history and progression risk of cervical intraepithelial neoplasia.

Pilot questions 2.1

- Describe cervical polyps and their management. (Linked to SLO 2.1)
- Describe cervical ectropion and its clinical significance. (Linked to SLO 2.1)
- Describe the classification of cervical intraepithelial neoplasia by grade. (Linked to SLO 2.2)
- Describe the natural history of low-grade versus high-grade CIN. (Linked to SLO 2.2)
- List the risk factors for cervical cancer. (Linked to SLO 2.2)

2.2 Cervical Cancer: Presentation, Diagnosis, and Staging

2.2.1 Epidemiology, aetiology, and clinical presentation

Cervical cancer predominantly affects women in their reproductive and perimenopausal years, with squamous cell carcinoma accounting for the great majority of cases and adenocarcinoma, arising from the endocervical glandular epithelium, accounting for a smaller but genuinely

important minority, both sharing the same underlying aetiological pathway of persistent high-risk HPV infection driving progressive epithelial dysplasia and, eventually, invasive malignancy.

Early cervical cancer may be entirely asymptomatic, detected only through routine cervical screening, while more established disease typically presents with abnormal vaginal bleeding, particularly post-coital or intermenstrual bleeding, and, in more advanced disease, offensive vaginal discharge, pelvic pain, and, where local structures are involved, symptoms suggestive of bladder or bowel infiltration, underscoring why persistent post-coital bleeding in particular should never be dismissed without appropriate examination.

Fill in the blank: Squamous cell carcinoma accounts for the great majority of cervical cancer cases, with _____ accounting for a smaller but important minority. Persistent post-coital bleeding should never be dismissed without appropriate _____.

2.2.2 Examination under anaesthesia, biopsy, and diagnostic workup

Examination under anaesthesia (EUA) allows thorough, systematic assessment of the extent of local disease, including bimanual and rectal examination to assess parametrial involvement, without the limitation of patient discomfort or muscle guarding that can restrict adequate assessment in the awake patient, and is frequently combined with cervical biopsy, cystoscopy, and, where indicated, proctoscopy to comprehensively assess the local extent of disease before finalising staging.

Cervical biopsy (either a targeted punch biopsy or a larger cone biopsy where a more substantial tissue sample is required for accurate diagnosis and microinvasion assessment) provides definitive histological confirmation of malignancy and, importantly, information about tumour grade and, in early-stage disease, the depth and lateral extent of any microinvasion identified, findings that directly and substantially influence subsequent staging and treatment planning.

Fill in the blank: Examination under anaesthesia allows thorough assessment of parametrial involvement by bimanual and _____ examination. Cervical biopsy provides definitive histological confirmation and information about tumour _____.

2.2.3 Staging of cervical cancer

Cervical cancer staging follows the International Federation of Gynecology and Obstetrics (FIGO) system, now incorporating both clinical assessment and imaging findings, ranging from stage I (confined to the cervix) through stage II (extending beyond the cervix but not to the pelvic wall or lower third of the vagina), stage III (extending to the pelvic wall, lower third of the vagina, or causing hydronephrosis), to stage IV (extending beyond the true pelvis or involving the bladder or rectal mucosa).

Accurate staging directly determines the recommended treatment approach and provides essential prognostic information, with modern staging increasingly incorporating cross-sectional imaging, particularly MRI, to more accurately assess parametrial and nodal involvement than

clinical examination alone can reliably achieve, reflecting a genuine, welcome evolution in staging practice towards a more objective, imaging-supported assessment of disease extent.

Fill in the blank: FIGO stage III cervical cancer involves extension to the pelvic wall, lower third of the vagina, or causing _____. Modern cervical cancer staging increasingly incorporates cross-sectional imaging, particularly _____, to assess parametrial and nodal involvement.

Stage	Extent of Disease
Stage I	Carcinoma confined to the cervix (extension to corpus disregarded)
Stage II	Carcinoma extends beyond cervix but not to pelvic wall or lower third of vagina
Stage III	Carcinoma extends to pelvic wall and/or involves lower third of vagina and/or causes hydronephrosis/non-functioning kidney
Stage IV	Carcinoma extends beyond true pelvis or clinically involves bladder/rectal mucosa; distant metastasis

Table 2.2: FIGO staging system for cervical cancer.

Pilot questions 2.2

1. Describe the epidemiology and histological subtypes of cervical cancer. (Linked to SLO 2.3)
2. Describe the clinical presentation of cervical cancer. (Linked to SLO 2.3)
3. Describe the purpose and components of examination under anaesthesia in cervical cancer diagnosis. (Linked to SLO 2.4)
4. Describe the role of cervical biopsy in diagnostic workup. (Linked to SLO 2.4)
5. List the FIGO stages of cervical cancer. (Linked to SLO 2.5)

2.3 Cervical Cancer: Treatment, Prognosis, and Prevention

2.3.1 Treatment modalities in cervical cancer

Treatment of cervical cancer is genuinely stage-dependent: early-stage disease (stage I and selected stage II) is generally treated surgically, with options ranging from cone biopsy or simple hysterectomy for very early microinvasive disease to radical hysterectomy with pelvic lymphadenectomy for more established early-stage disease, aiming to achieve cure while preserving, wherever oncologically appropriate, the woman's fertility in carefully selected younger women.

More advanced disease (locally advanced stage II to stage IVA) is generally treated with concurrent chemoradiotherapy, combining external beam radiotherapy, brachytherapy, and concurrent platinum-based chemotherapy to enhance radiosensitivity, an approach that has become the established standard of care for locally advanced cervical cancer given robust evidence of improved outcomes compared with radiotherapy alone.

Fill in the blank: Early-stage cervical cancer is generally treated surgically, ranging from cone biopsy to radical hysterectomy with pelvic _____. Locally advanced cervical cancer is generally treated with concurrent chemoradiotherapy, combining radiotherapy with platinum-based _____.

2.3.2 Palliative care and prognosis

Palliative care for advanced or recurrent cervical cancer focuses on symptom control, including management of pain, vaginal bleeding or discharge, and, where relevant, symptoms from ureteric obstruction or fistula formation, alongside genuine psychological and spiritual support for the woman and her family, delivered as an integrated, holistic component of care rather than a service reserved only for the final days of life.

Prognosis in cervical cancer is closely related to stage at diagnosis, with five-year survival considerably higher for early-stage, localised disease than for advanced or metastatic disease, a relationship that directly underscores why early detection through effective screening, and prompt investigation of symptoms such as post-coital bleeding, matters so profoundly for improving overall outcomes at a population level.

Fill in the blank: Palliative care for advanced cervical cancer includes management of pain, bleeding, and symptoms from ureteric obstruction or _____ formation. Five-year survival in cervical cancer is considerably higher for early-stage, _____ disease.

2.3.3 Prevention of cervical cancer

Primary prevention of cervical cancer centres on HPV vaccination, ideally delivered before the onset of sexual activity given its greatest effectiveness when administered prior to any exposure to the virus, targeting the high-risk HPV types responsible for the great majority of cervical

cancer cases, and representing one of the most genuinely powerful, evidence-based cancer prevention interventions available in the whole of modern medicine.

Secondary prevention through organised cervical screening, whether by cytology or, increasingly, primary HPV testing, allows detection and treatment of pre-malignant CIN before progression to invasive cancer occurs, and expanding both HPV vaccination coverage and screening access in Nigeria specifically represents a genuinely achievable, high-value public health priority given the substantial, largely preventable burden of cervical cancer the country continues to face.

Fill in the blank: HPV vaccination is ideally delivered before the onset of _____ activity, given its greatest effectiveness before any viral exposure. Secondary prevention through organised cervical screening allows detection and treatment of pre-malignant CIN before progression to _____ cancer.

Category	Details
Treatment by Stage	Stage I: surgery (radical hysterectomy, lymphadenectomy). Stage II–III: concurrent chemoradiation (cisplatin-based). Stage IV: systemic therapy, palliative radiotherapy.
Palliative Care Principles	Symptom control (pain, bleeding, discharge); psychosocial support; palliative radiotherapy for local symptoms; systemic therapy for advanced disease; holistic end-of-life care.
Primary Prevention	HPV vaccination (girls and boys before sexual debut); safe sexual practices; smoking cessation.
Secondary Prevention	Cervical screening (Pap smear, HPV DNA testing); VIA (visual inspection with acetic acid) in low-resource settings; early detection and treatment of precancerous lesions.

Box 2.3: Cervical cancer treatment by stage, palliative care, and prevention strategies.

Pilot questions 2.3

1. Describe the treatment approach for early-stage cervical cancer. (Linked to SLO 2.6)
2. Describe the treatment approach for locally advanced cervical cancer. (Linked to SLO 2.6)
3. Describe the principles of palliative care in advanced or recurrent cervical cancer. (Linked to SLO 2.7)

4. Explain the relationship between stage at diagnosis and prognosis in cervical cancer. (Linked to SLO 2.7)
5. Describe the primary and secondary prevention strategies for cervical cancer. (Linked to SLO 2.7)

Series Summary

This Series has covered disorders of the cervix and the precursors to cervical cancer, including cervical intraepithelial neoplasia, followed by cervical cancer presentation, diagnosis, and staging. It concluded with cervical cancer treatment, palliative care, prognosis, and prevention.

You should now be able to describe benign cervical lesions, enumerate cervical cancer incidence, precursors, and risk factors, explain its epidemiology and presentation, discuss diagnostic workup and staging, list treatment modalities, and describe palliative care, prognosis, and prevention (Linked to SLOs 2.1 to 2.7).

Glossary of Terms

1. **Cervical ectropion:** eversion of the columnar epithelium of the endocervical canal onto the visible surface of the cervix, a physiological finding.
2. **Cervical intraepithelial neoplasia (CIN):** the pre-malignant precursor to cervical squamous cell carcinoma, graded 1 to 3 by depth of epithelial involvement.
3. **Cervical polyp:** the most common benign cervical lesion, arising from the endocervical canal.
4. **Chemoradiotherapy:** combined treatment using radiotherapy and concurrent chemotherapy, standard for locally advanced cervical cancer.
5. **Cone biopsy:** excisional cervical biopsy providing a larger tissue sample for diagnosis and microinvasion assessment.
6. **Examination under anaesthesia (EUA):** systematic clinical assessment of cervical cancer extent performed under anaesthesia.
7. **FIGO staging:** the International Federation of Gynecology and Obstetrics staging system for cervical cancer.

8. **Radical hysterectomy:** extensive surgical removal of the uterus and surrounding tissue, used in early-stage cervical cancer.
9. **Adenocarcinoma:** a cervical cancer histological subtype arising from the endocervical glandular epithelium.
10. **Brachytherapy:** internal radiotherapy delivered close to or within the tumour, used in cervical cancer treatment.
11. **Parametrial involvement:** extension of cervical cancer into the tissue surrounding the cervix, assessed on examination and imaging.
12. **Microinvasion:** early, minimal invasion of cervical cancer into the underlying stroma, assessed histologically.

Concept Check Questions [Series 2]

Objective questions

1. Cervical polyps are generally managed by simple _____ in the outpatient clinic.
2. CIN is classified by depth of epithelial involvement into CIN 1, CIN 2, and CIN _____.
3. Persistent infection with high-risk _____ is established as the necessary underlying cause of cervical cancer.
4. FIGO stage III cervical cancer involves extension to the pelvic wall, lower third of the vagina, or causing _____.
5. HPV vaccination is ideally delivered before the onset of _____ activity.

Short-answer questions

- Describe the natural history of low-grade versus high-grade CIN. (Linked to SLO 2.2)
- Describe the clinical presentation of cervical cancer. (Linked to SLO 2.3)
- Describe the role of cervical biopsy in diagnostic workup. (Linked to SLO 2.4)
- Explain the relationship between stage at diagnosis and prognosis in cervical cancer. (Linked to SLO 2.7)

- Describe the primary and secondary prevention strategies for cervical cancer. (Linked to SLO 2.7)

Long-answer questions

1. Describe benign lesions of the cervix and the classification and natural history of CIN. (Linked to SLO 2.1, SLO 2.2)
2. Describe the epidemiology, aetiology, and clinical presentation of cervical cancer. (Linked to SLO 2.3)
3. Describe the diagnostic workup and staging of cervical cancer. (Linked to SLO 2.4, SLO 2.5)
4. List the treatment modalities in cervical cancer according to stage. (Linked to SLO 2.6)
5. Describe palliative care, prognosis, and prevention of cervical cancer. (Linked to SLO 2.7)

Answers to Concept Check Questions [Series 2]

Objective questions

6. Avulsion.
7. 3.
8. HPV.
9. Hydronephrosis.
10. Sexual.

Short-answer questions

11. Low-grade CIN 1 frequently regresses spontaneously; high-grade CIN 2 and 3 carry substantially greater risk of persistence or progression.
12. Early disease may be asymptomatic; established disease typically presents with post-coital or intermenstrual bleeding, and later, discharge and pain.

13. Cervical biopsy provides definitive histological confirmation and information about tumour grade and microinvasion, guiding staging and treatment.
14. Five-year survival is considerably higher for early-stage, localised disease than for advanced or metastatic disease.
15. Primary prevention through HPV vaccination and secondary prevention through organised cervical screening.

Long-answer questions

16. **Basic response:** Cervical polyps and ectropion are common benign findings, while CIN represents the pre-malignant spectrum with variable natural history by grade.

Value-added response: Low-grade CIN often regresses spontaneously, while high-grade CIN carries substantial progression risk, directly guiding surveillance versus treatment decisions.

17. **Basic response:** Cervical cancer predominantly affects reproductive-age women, driven by persistent high-risk HPV infection, presenting with abnormal bleeding, particularly post-coital.

Value-added response: Persistent post-coital bleeding should never be dismissed without examination, given its association with cervical malignancy.

18. **Basic response:** Diagnostic workup combines examination under anaesthesia and biopsy, with FIGO staging from confined disease through to distant extension.

Value-added response: Modern staging increasingly incorporates cross-sectional imaging for more accurate assessment of parametrial and nodal involvement.

19. **Basic response:** Early-stage disease is treated surgically, while locally advanced disease is treated with concurrent chemoradiotherapy.

Value-added response: Treatment aims to preserve fertility in carefully selected younger women with early-stage disease where oncologically appropriate.

20. **Basic response:** Palliative care addresses symptom control and psychological support, with prognosis closely related to stage at diagnosis.

Value-added response: HPV vaccination and organised screening together represent the most powerful, evidence-based strategies for preventing cervical cancer.

Answers to Pilot Questions [Series 2]

Part 2.1

11. The most common benign cervical lesion, generally managed by simple avulsion with histology to exclude malignant change.
12. Eversion of columnar epithelium onto the cervix, physiological, generally asymptomatic, not requiring treatment once malignancy excluded.
13. CIN 1 (lower third), CIN 2 (middle third), and CIN 3 (full thickness) of the epithelium.
14. Low-grade CIN 1 often regresses spontaneously; high-grade CIN 2 and 3 carry greater risk of persistence or progression.
15. Persistent high-risk HPV, early first intercourse, multiple partners, smoking, immunosuppression, and lack of screening.

Part 2.2

1. Predominantly squamous cell carcinoma, with adenocarcinoma a smaller but important minority, both driven by persistent HPV infection.
2. May be asymptomatic early; established disease presents with post-coital or intermenstrual bleeding, and later discharge and pain.
3. Systematic assessment of local extent, including bimanual and rectal examination for parametrial involvement.
4. Provides definitive histological confirmation and information on tumour grade and microinvasion, guiding staging and treatment.
5. Stage I (confined to cervix), stage II, stage III (pelvic wall or hydronephrosis), and stage IV.

Part 2.3

6. Surgical treatment, ranging from cone biopsy to radical hysterectomy with pelvic lymphadenectomy, with fertility preservation where appropriate.
7. Concurrent chemoradiotherapy, combining external beam radiotherapy, brachytherapy, and platinum-based chemotherapy.
8. Symptom control for pain, bleeding, and obstruction or fistula, alongside psychological and spiritual support.
9. Five-year survival is considerably higher for early-stage, localised disease than advanced or metastatic disease.
10. HPV vaccination as primary prevention, and organised cervical screening as secondary prevention.

References and Attributions [Series 2]

Textual References

11. Hoffman, B. L., Schorge, J. O., Halvorson, L. M. et al. (2020). Williams Gynecology (4th ed.). McGraw Hill.
12. International Federation of Gynecology and Obstetrics (2021). FIGO Cancer Report. FIGO.
13. World Health Organization (2021). WHO Guideline for Screening and Treatment of Cervical Pre-Cancer Lesions for Cervical Cancer Prevention (2nd ed.). WHO Press.
14. National Comprehensive Cancer Network (2023). NCCN Clinical Practice Guidelines in Oncology: Cervical Cancer. NCCN.

Figures, Plates, Tables, and Boxes

1. Figure 2.1: Natural history and progression risk of cervical intraepithelial neoplasia. AI-generated using the prompt: "Create a professional medical diagram titled Natural History of Cervical Intraepithelial Neoplasia, showing progression stages with regression and progression rates. Clean clinical educational diagram style."
2. Table 2.2: FIGO staging system for cervical cancer. AI-generated using the prompt: "Create a clean reference table titled FIGO Staging of Cervical Cancer, listing stages I

through IV with defining extent of disease. Simple clinical reference table style with outside border."

3. Box 2.3: Cervical cancer treatment by stage, palliative care, and prevention strategies. AI-generated using the prompt: "Create a simple single-column reference box with an outside border titled Cervical Cancer: Treatment and Prevention, listing treatment by stage, palliative care, and prevention. Clinical reference box style.

Course code: OBG 506

Course title: Gynaecological Oncology

Course credit load: 1 Unit

Series 3: Uterine and Ovarian Tumours

- **Part 3.1: Disorders of the Uterus**
    - Sub Part 3.1.1: Benign lesions of the uterus
    - Sub Part 3.1.2: Pre-malignant lesions of the uterus
    - Sub Part 3.1.3: Epidemiology of endometrial cancer
- **Part 3.2: Endometrial Cancer**
    - Sub Part 3.2.1: Clinical presentation and diagnostic workup
    - Sub Part 3.2.2: Staging of endometrial cancer
    - Sub Part 3.2.3: Treatment options for endometrial cancer
- **Part 3.3: Ovarian Tumours**
    - Sub Part 3.3.1: Benign, borderline, and malignant ovarian lesions: epidemiology
    - Sub Part 3.3.2: Evaluation of ovarian neoplasms
    - Sub Part 3.3.3: Staging, treatment, and follow-up of ovarian cancer

Introduction

In the last Series, we explored cervical disorders and cancer. We now turn to two further organs at the heart of gynaecological oncology: the uterus, home to the most common gynaecological malignancy in many settings, and the ovary, whose cancer remains notoriously difficult to detect early, often presenting only once disease has already spread beyond the pelvis. This Series builds the knowledge you need to recognise, evaluate, stage, and treat both uterine and ovarian tumours.

The aim of this Series is to equip you with a thorough understanding of benign and pre-malignant uterine disease, endometrial cancer, and the full spectrum of benign, borderline, and malignant ovarian tumours.

We shall commence this Series by examining disorders of the uterus, including benign and pre-malignant lesions and the epidemiology of endometrial cancer. Next, we will consider endometrial cancer presentation, diagnosis, staging, and treatment. Finally, we will conclude by examining ovarian tumours, their epidemiology, evaluation, staging, and treatment.

Series Learning Outcomes

Upon completing this Series, you should be able to:

- **SLO 3.1:** describe benign and pre-malignant lesions of the uterus,
- **SLO 3.2:** describe the epidemiology of endometrial cancer,
- **SLO 3.3:** discuss the clinical presentation and diagnostic workup of endometrial cancer,
- **SLO 3.4:** list treatment options for endometrial cancer,
- **SLO 3.5:** explain the benign, borderline, and malignant lesions of the ovary regarding epidemiology,
- **SLO 3.6:** list risk factors, available screening tests, diagnosis, and prevention of ovarian cancer, and
- **SLO 3.7:** outline staging of malignant ovarian disease, prognostic factors, methods of treatment, and follow-up.

3.1 Disorders of the Uterus

3.1.1 Benign lesions of the uterus

Uterine fibroids (leiomyomas) are the most common benign uterine tumour, arising from the myometrium, classified by location as submucosal, intramural, or subserosal, presenting with heavy menstrual bleeding, pelvic pressure or pain, and, depending on size and location, subfertility, with the specific symptom profile and management approach substantially influenced by fibroid location, number, and size.

Endometrial polyps are localised overgrowths of endometrial tissue projecting into the uterine cavity, presenting with abnormal uterine bleeding, particularly intermenstrual bleeding or postmenopausal bleeding, generally diagnosed by transvaginal ultrasound or hysteroscopy and managed by hysteroscopic polypectomy with histological examination to exclude the rare possibility of underlying malignant change.

Fill in the blank: Uterine fibroids are classified by location as submucosal, intramural, or _____. Endometrial polyps are generally diagnosed by transvaginal ultrasound or _____.

3.1.2 Pre-malignant lesions of the uterus

Endometrial hyperplasia (excessive proliferation of the endometrial glands relative to stroma, resulting from unopposed oestrogen stimulation) is the recognised pre-malignant precursor to endometrial cancer, classified as hyperplasia without atypia (a low risk of progression to malignancy) or atypical hyperplasia (a substantially higher risk of progression, and frequently coexisting with an already established, undetected endometrial cancer at the time of diagnosis).

Risk factors for endometrial hyperplasia mirror those for endometrial cancer itself, including obesity (through peripheral aromatisation of androgens to oestrogen in adipose tissue), polycystic ovary syndrome (through chronic anovulation and unopposed oestrogen exposure), unopposed oestrogen therapy, and tamoxifen use, each reflecting the shared underlying mechanism of prolonged, unopposed oestrogen exposure to the endometrium.

Fill in the blank: Atypical endometrial hyperplasia carries a substantially higher risk of progression and frequently coexists with an already established, undetected endometrial _____. Obesity increases endometrial hyperplasia risk through peripheral aromatisation of androgens to _____ in adipose tissue.

3.1.3 Epidemiology of endometrial cancer

Endometrial cancer is the most common gynaecological malignancy in many high-income countries, predominantly affecting postmenopausal women, with incidence rising in Nigeria and other low- and middle-income countries alongside increasing rates of obesity, the single most significant modifiable risk factor for this specific malignancy given its central role in driving unopposed oestrogen exposure to the endometrium.

Endometrial cancer is broadly classified into two types with distinct epidemiological and prognostic characteristics: type I (oestrogen-dependent, endometrioid histology, generally lower grade and better prognosis, associated with obesity and unopposed oestrogen exposure) and type II (oestrogen-independent, including serous and clear cell histology, generally higher grade and poorer prognosis, occurring in older, often thinner women without the typical type I risk factor profile).

Fill in the blank: Obesity is the single most significant modifiable risk factor for endometrial cancer given its role in driving unopposed _____ exposure. Type II endometrial cancer is oestrogen-independent, occurring in older women, and is generally higher _____ with poorer prognosis.

Feature	Type I	Type II
Histology	**Endometrioid adenocarcinoma (most common)**	**Serous carcinoma, clear cell carcinoma**
Hormone Dependence	**Estrogen-dependent; often arises in setting of unopposed estrogen**	**Estrogen-independent; not linked to hormonal stimulation**
Patient Profile	**Perimenopausal/postmenopausal women; history of obesity, diabetes, PCOS, estrogen therapy**	**Older, postmenopausal women; often without classic risk factors**
Prognosis	**Generally favorable; lower grade, less aggressive**	**Poorer prognosis; high grade, aggressive, early spread**

Table 3.1: Comparison of type I and type II endometrial cancer.

Pilot questions 3.1

- Describe uterine fibroids and their classification by location. (Linked to SLO 3.1)
- Describe endometrial polyps and their management. (Linked to SLO 3.1)
- Describe endometrial hyperplasia and its classification. (Linked to SLO 3.1)
- List the risk factors for endometrial hyperplasia and endometrial cancer. (Linked to SLO 3.2)
- Compare type I and type II endometrial cancer. (Linked to SLO 3.2)

3.2 Endometrial Cancer

3.2.1 Clinical presentation and diagnostic workup

Postmenopausal bleeding is the cardinal presenting symptom of endometrial cancer, present in the great majority of cases at diagnosis, meaning any woman with postmenopausal bleeding warrants prompt investigation to exclude this diagnosis, given that endometrial cancer is identified in a genuinely significant proportion of women presenting with this specific symptom, particularly with increasing age.

Diagnostic workup begins with transvaginal ultrasound measurement of endometrial thickness, with a thin endometrium considerably reassuring against malignancy, followed by endometrial sampling, either by outpatient pipelle biopsy or, where this is inadequate, non-diagnostic, or clinical suspicion remains high despite a normal result, by hysteroscopy with directed biopsy, providing definitive histological diagnosis.

Fill in the blank: Postmenopausal bleeding is the cardinal presenting symptom of endometrial cancer, present in the great majority of cases at _____. Diagnostic workup begins with transvaginal ultrasound measurement of endometrial _____.

3.2.2 Staging of endometrial cancer

Endometrial cancer staging follows the FIGO system, primarily surgical rather than purely clinical, ranging from stage I (confined to the uterine body) through stage II (extending to the cervical stroma) and stage III (local or regional spread, including to the serosa, adnexa, vagina, or pelvic and para-aortic lymph nodes) to stage IV (invading bladder or bowel mucosa, or distant metastasis).

Surgical staging (total hysterectomy with bilateral salpingo-oophorectomy, together with pelvic and, where indicated, para-aortic lymph node assessment) provides the definitive information on which stage, and, correspondingly, the need for any adjuvant treatment, is ultimately based, reflecting the genuinely central role surgery plays in both the treatment and the accurate staging of endometrial cancer.

Fill in the blank: Endometrial cancer staging is primarily _____ rather than purely clinical. Surgical staging includes total hysterectomy with bilateral _____, together with lymph node assessment.

3.2.3 Treatment options for endometrial cancer

Surgery (total hysterectomy with bilateral salpingo-oophorectomy and staging lymph node assessment) is the primary treatment for the great majority of endometrial cancer cases, generally performed by minimally invasive laparoscopic or robotic approach where feasible, given the recognised benefits of reduced perioperative morbidity compared with open surgery in appropriately selected women.

Adjuvant treatment (radiotherapy, and, for higher-risk or advanced disease, chemotherapy) is guided by surgical stage and identified pathological risk factors, such as high tumour grade, deep myometrial invasion, or lymphovascular space invasion, while progestogen-based fertility-preserving treatment may be considered for carefully selected young women with early, low-grade, hormone-sensitive disease who strongly wish to preserve fertility, always following genuinely thorough counselling on the associated risks.

Fill in the blank: Surgery is generally performed by minimally invasive laparoscopic or _____ approach where feasible. Progestogen-based fertility-preserving treatment may be

considered for carefully selected young women with early, low-grade, hormone-_____ disease.

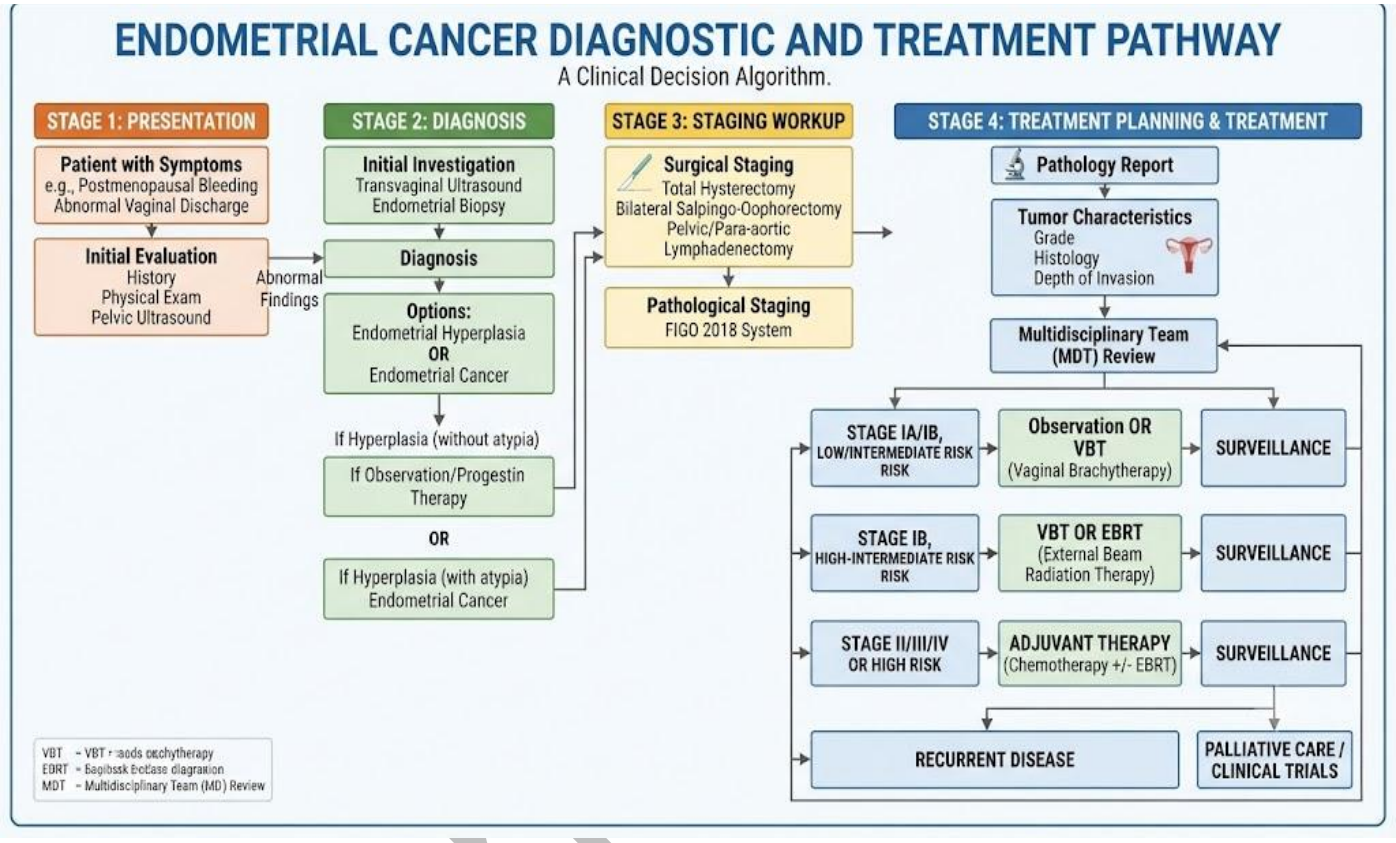

Figure 3.2: Diagnostic and treatment pathway for endometrial cancer.

Pilot questions 3.2

1. Explain why postmenopausal bleeding warrants prompt investigation. (Linked to SLO 3.3)
2. Describe the diagnostic workup for suspected endometrial cancer. (Linked to SLO 3.3)
3. Describe the FIGO staging system for endometrial cancer. (Linked to SLO 3.3)
4. Describe the components of surgical staging for endometrial cancer. (Linked to SLO 3.3)
5. List the treatment options for endometrial cancer. (Linked to SLO 3.4)

3.3 Ovarian Tumours

3.3.1 Benign, borderline, and malignant ovarian lesions: epidemiology

Ovarian neoplasms span a genuinely broad spectrum from entirely benign (the great majority of ovarian masses in premenopausal women, including simple functional cysts and benign teratomas) through borderline tumours (an intermediate category with atypical proliferative features but lacking genuine stromal invasion, carrying a favourable prognosis even when treated conservatively) to frankly malignant disease, with the relative proportion of each category shifting substantially with increasing age.

Ovarian cancer occurs predominantly in postmenopausal women, with epithelial tumours accounting for the great majority of malignant cases, and germ cell and sex cord-stromal tumours accounting for a smaller proportion, occurring more typically in younger women, a distinction of genuine clinical importance given the meaningfully different treatment approach and generally more favourable prognosis associated with these less common histological subtypes.

Fill in the blank: Borderline ovarian tumours have atypical proliferative features but lack genuine stromal _____. Epithelial tumours account for the great majority of malignant ovarian cases, occurring predominantly in _____ women.

3.3.2 Evaluation of ovarian neoplasms

Risk factors for ovarian cancer include increasing age, nulliparity, early menarche and late menopause (reflecting cumulative ovulation exposure), a family history of ovarian or breast cancer (particularly with a known BRCA1 or BRCA2 mutation), and endometriosis, while factors reducing risk include combined oral contraceptive use, multiparity, and breastfeeding, each reflecting reduced cumulative ovulatory exposure over a woman's reproductive lifetime.

Evaluation of a suspected ovarian mass combines transvaginal ultrasound assessment of morphological features suggestive of malignancy with serum tumour markers, most commonly CA-125 in postmenopausal women, with a structured risk-of-malignancy scoring system combining these ultrasound and biochemical findings directly guiding the urgency of further management and the specific pathway of onward referral, given that no single screening test has yet been shown to reliably reduce ovarian cancer mortality at a population level.

Fill in the blank: Risk factors for ovarian cancer include a family history of ovarian or breast cancer, particularly with a known BRCA1 or _____ mutation. Evaluation of a suspected ovarian mass combines ultrasound with serum tumour markers, most commonly _____ in postmenopausal women.

3.3.3 Staging, treatment, and follow-up of ovarian cancer

Ovarian cancer staging follows the FIGO system, primarily surgical, ranging from stage I (confined to the ovary or ovaries) through stage II (pelvic extension) and stage III (peritoneal spread beyond the pelvis or retroperitoneal lymph node involvement) to stage IV (distant metastasis), with the great majority of women unfortunately presenting with advanced, stage III or IV disease given the historically limited effectiveness of screening and the often vague, non-specific early symptoms of this particular malignancy.

Treatment combines cytoreductive (debulking) surgery, aiming to remove all visible tumour wherever possible, with platinum-based chemotherapy, with the specific sequence, primary surgery followed by chemotherapy or, in some cases, neoadjuvant chemotherapy followed by interval surgery, individualised according to disease extent and the woman's overall fitness for surgery, alongside structured, sustained follow-up given the recognised, substantial risk of recurrence even after apparently successful initial treatment.

Fill in the blank: Ovarian cancer staging follows the FIGO system and is primarily _____. Treatment combines cytoreductive surgery with platinum-based _____, individualised according to disease extent and fitness for surgery.

Category	Details
Categories	Benign (functional cysts, serous/mucinous cystadenomas, dermoid cysts); Borderline (low malignant potential tumours); Malignant (epithelial ovarian carcinoma, germ cell tumours, sex-cord stromal tumours)
Risk Factors	Family history (BRCA1/2 mutations, Lynch syndrome), nulliparity, early menarche, late menopause, endometriosis, age
Evaluation	Clinical exam; pelvic ultrasound (solid/cystic features, septations, Doppler flow); tumour markers (CA-125, AFP, β-hCG, LDH); CT/MRI for staging; histopathology for definitive diagnosis
Staging & Treatment Principles	FIGO staging system; surgery (staging laparotomy, cytoreduction); chemotherapy (platinum-based for epithelial cancers); fertility-sparing surgery in selected young patients; targeted therapy (PARP inhibitors in BRCA mutation carriers); multidisciplinary management

Box 3.3: Ovarian tumour categories, risk factors, evaluation, and treatment.

Pilot questions 3.3

1. Describe the spectrum of ovarian neoplasms from benign through borderline to malignant. (Linked to SLO 3.5)
2. Describe the histological subtypes of ovarian cancer and their typical age distribution. (Linked to SLO 3.5)
3. List the risk factors and protective factors for ovarian cancer. (Linked to SLO 3.6)
4. Describe the evaluation of a suspected ovarian mass. (Linked to SLO 3.6)
5. Describe the staging and treatment of ovarian cancer. (Linked to SLO 3.7)

Series Summary

This Series has covered disorders of the uterus, including benign and pre-malignant lesions and the epidemiology of endometrial cancer, followed by endometrial cancer presentation, diagnosis, staging, and treatment. It concluded with ovarian tumours, their epidemiology, evaluation, staging, and treatment.

You should now be able to describe benign and pre-malignant uterine lesions, describe endometrial cancer epidemiology, presentation, and workup, list its treatment options, explain the epidemiology of ovarian tumours, list ovarian cancer risk factors and evaluation, and outline its staging, treatment, and follow-up (Linked to SLOs 3.1 to 3.7).

Glossary of Terms

1. **Borderline ovarian tumour:** a tumour with atypical proliferative features but lacking genuine stromal invasion, carrying a favourable prognosis.
2. **CA-125:** a serum tumour marker used, alongside ultrasound findings, in the evaluation of a suspected ovarian mass.
3. **Cytoreductive (debulking) surgery:** surgery aiming to remove all visible tumour in ovarian cancer treatment.
4. **Endometrial hyperplasia:** excessive proliferation of the endometrial glands relative to stroma, the pre-malignant precursor to endometrial cancer.
5. **Fibroid (leiomyoma):** the most common benign uterine tumour, arising from the myometrium.
6. **Risk of malignancy index:** a scoring system combining ultrasound features and tumour markers to guide management of an ovarian mass.
7. **Type I endometrial cancer:** oestrogen-dependent, endometrioid histology, generally lower grade with better prognosis.
8. **Type II endometrial cancer:** oestrogen-independent, including serous and clear cell histology, generally higher grade with poorer prognosis.
9. **Endometrial polyp:** a localised overgrowth of endometrial tissue projecting into the uterine cavity.
10. **BRCA1 and BRCA2:** genes associated with a hereditary predisposition to ovarian and breast cancer when mutated.

11. **Neoadjuvant chemotherapy:** chemotherapy given before surgery, used in selected ovarian cancer cases before interval debulking surgery.
12. **Lymphovascular space invasion:** invasion of tumour cells into lymphatic or vascular spaces, a pathological risk factor guiding adjuvant treatment.

Concept Check Questions [Series 3]

Objective questions

1. Uterine fibroids are classified by location as submucosal, intramural, or _____.
2. Obesity increases endometrial hyperplasia risk through peripheral aromatisation of androgens to _____ in adipose tissue.
3. Postmenopausal bleeding is the cardinal presenting symptom of endometrial cancer, present in the great majority of cases at _____.
4. Borderline ovarian tumours have atypical proliferative features but lack genuine stromal _____.
5. Evaluation of a suspected ovarian mass combines ultrasound with serum tumour markers, most commonly _____ in postmenopausal women.

Short-answer questions

- Compare type I and type II endometrial cancer. (Linked to SLO 3.2)
- Describe the components of surgical staging for endometrial cancer. (Linked to SLO 3.3)
- List the treatment options for endometrial cancer. (Linked to SLO 3.4)
- Describe the histological subtypes of ovarian cancer and their typical age distribution. (Linked to SLO 3.5)
- List the risk factors and protective factors for ovarian cancer. (Linked to SLO 3.6)

Long-answer questions

1. Describe benign and pre-malignant lesions of the uterus and the epidemiology of endometrial cancer. (Linked to SLO 3.1, SLO 3.2)
2. Describe the clinical presentation, diagnostic workup, and staging of endometrial cancer. (Linked to SLO 3.3)
3. List the treatment options for endometrial cancer. (Linked to SLO 3.4)
4. Describe the epidemiology and evaluation of benign, borderline, and malignant ovarian tumours. (Linked to SLO 3.5, SLO 3.6)
5. Describe the staging, treatment, and follow-up of ovarian cancer. (Linked to SLO 3.7)

Answers to Concept Check Questions [Series 3]

Objective questions

6. Subserosal.
7. Oestrogen.
8. Diagnosis.
9. Invasion.
10. CA-125.

Short-answer questions

11. Type I is oestrogen-dependent, endometrioid, lower grade with better prognosis; type II is oestrogen-independent, higher grade with poorer prognosis.
12. Total hysterectomy with bilateral salpingo-oophorectomy and pelvic and, where indicated, para-aortic lymph node assessment.
13. Surgery as primary treatment, adjuvant radiotherapy or chemotherapy for higher-risk disease, and progestogen-based fertility preservation in selected cases.
14. Epithelial tumours predominate in postmenopausal women; germ cell and sex cord-stromal tumours occur more typically in younger women.
15. Risk factors include age, nulliparity, early menarche, late menopause, and BRCA mutation; protective factors include contraceptive use and breastfeeding.

Long-answer questions

16. **Basic response:** Uterine fibroids and endometrial polyps are common benign findings, while endometrial hyperplasia is the pre-malignant precursor with variable progression risk by subtype.

Value-added response: Endometrial cancer epidemiology is closely tied to obesity and unopposed oestrogen exposure, with type I and type II disease carrying distinct prognosis.

17. **Basic response:** Endometrial cancer presents predominantly with postmenopausal bleeding, diagnosed by ultrasound and biopsy, and staged surgically following FIGO criteria.

Value-added response: Surgical staging provides the definitive basis for adjuvant treatment decisions, reflecting the central role of surgery in both diagnosis and treatment.

18. **Basic response:** Treatment is primarily surgical, with adjuvant radiotherapy or chemotherapy guided by pathological risk factors, and fertility preservation considered in selected young women.

Value-added response: Progestogen-based fertility-preserving treatment requires thorough counselling on associated risks before proceeding.

19. **Basic response:** Ovarian tumours span benign, borderline, and malignant categories, with epithelial cancer predominating in older women and evaluated using ultrasound and tumour markers.

Value-added response: No single screening test has been shown to reliably reduce ovarian cancer mortality, making structured risk assessment essential.

20. **Basic response:** Ovarian cancer staging is surgical, with the majority presenting at advanced stage, treated with cytoreductive surgery and platinum-based chemotherapy.

Value-added response: Sustained follow-up is essential given the substantial recurrence risk even after apparently successful initial treatment.

Answers to Pilot Questions [Series 3]

Part 3.1

11. The most common benign uterine tumour, classified as submucosal, intramural, or subserosal by location.
12. Localised endometrial overgrowths presenting with abnormal bleeding, diagnosed by ultrasound or hysteroscopy and managed by polypectomy.
13. Excessive endometrial gland proliferation, classified as hyperplasia without atypia or atypical hyperplasia.
14. Obesity, polycystic ovary syndrome, unopposed oestrogen therapy, and tamoxifen use.
15. Type I is oestrogen-dependent with better prognosis; type II is oestrogen-independent with poorer prognosis.

Part 3.2

1. Endometrial cancer is identified in a genuinely significant proportion of women presenting with this symptom, particularly with age.
2. Transvaginal ultrasound measurement of endometrial thickness, followed by pipelle biopsy or hysteroscopy with directed biopsy.
3. Stage I (confined to uterine body), stage II (cervical stroma), stage III (local or regional spread), and stage IV.
4. Total hysterectomy with bilateral salpingo-oophorectomy and pelvic and para-aortic lymph node assessment.
5. Surgery, adjuvant radiotherapy or chemotherapy, and progestogen-based fertility preservation in selected cases.

Part 3.3

6. Benign (the majority in premenopausal women), borderline (atypical but non-invasive), and malignant categories.
7. Epithelial tumours predominate in postmenopausal women; germ cell and sex cord-stromal tumours occur more in younger women.
8. Age, nulliparity, early menarche, late menopause, family history and BRCA mutation, and endometriosis; protective factors include contraceptive use.

9. Transvaginal ultrasound assessment of morphology combined with serum tumour markers, most commonly CA-125.
10. Surgical FIGO staging, with cytoreductive surgery and platinum-based chemotherapy, and sustained follow-up given recurrence risk.

References and Attributions [Series 3]

Textual References

11. Hoffman, B. L., Schorge, J. O., Halvorson, L. M. et al. (2020). Williams Gynecology (4th ed.). McGraw Hill.
12. International Federation of Gynecology and Obstetrics (2021). FIGO Cancer Report. FIGO.
13. National Comprehensive Cancer Network (2023). NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasms. NCCN.
14. National Comprehensive Cancer Network (2023). NCCN Clinical Practice Guidelines in Oncology: Ovarian Cancer. NCCN.

Figures, Plates, Tables, and Boxes

1. Table 3.1: Comparison of type I and type II endometrial cancer. AI-generated using the prompt: "Create a clean reference table titled Type I versus Type II Endometrial Cancer, comparing histology, hormone dependence, patient profile, and prognosis. Simple clinical reference table style with outside border."
2. Figure 3.2: Diagnostic and treatment pathway for endometrial cancer. AI-generated using the prompt: "Create a professional medical flowchart titled Endometrial Cancer Diagnostic and Treatment Pathway, showing the pathway from presentation through diagnosis and staging to treatment. Clean clinical educational diagram style."
3. Box 3.3: Ovarian tumour categories, risk factors, evaluation, and treatment. AI-generated using the prompt: "Create a simple single-column reference box with an outside border titled Ovarian Tumours Overview, listing categories, risk factors, evaluation, and treatment. Clinical reference box style."

Series 4: Gestational Trophoblastic Diseases

- **Part 4.1: Hydatidiform Mole**
    - Sub Part 4.1.1: Classification and pathophysiology of hydatidiform mole
    - Sub Part 4.1.2: Clinical presentation and diagnosis of hydatidiform mole
    - Sub Part 4.1.3: Management of hydatidiform mole
- **Part 4.2: Gestational Trophoblastic Neoplasia**
    - Sub Part 4.2.1: Invasive mole
    - Sub Part 4.2.2: Choriocarcinoma
    - Sub Part 4.2.3: Placental site trophoblastic tumour and epithelioid trophoblastic tumour
- **Part 4.3: Diagnosis, Staging, and Follow-up**
    - Sub Part 4.3.1: Role of serum beta-hCG in diagnosis and monitoring
    - Sub Part 4.3.2: Staging and risk scoring of gestational trophoblastic neoplasia
    - Sub Part 4.3.3: Treatment and follow-up, including contraception

Introduction

In the last Series, we explored uterine and ovarian tumours. We now turn to a genuinely unique corner of gynaecological oncology: gestational trophoblastic disease, a spectrum ranging from the relatively common, generally benign hydatidiform mole to the highly malignant, aggressively metastasising choriocarcinoma. What makes this Series so remarkable is that despite this aggressive behaviour, gestational trophoblastic neoplasia is among the most curable of all human malignancies, a genuinely encouraging story of oncological success built on the reliable biomarker beta-hCG and the characteristic chemosensitivity of trophoblastic tissue.

The aim of this Series is to equip you with a thorough understanding of hydatidiform mole, gestational trophoblastic neoplasia, and the diagnosis, staging, treatment, and follow-up of this disease spectrum.

We shall commence this Series by examining hydatidiform mole, its classification, presentation, diagnosis, and management. Next, we will consider gestational trophoblastic neoplasia, including invasive mole, choriocarcinoma, and the rarer placental site and epithelioid trophoblastic tumours. Finally, we will conclude by examining diagnosis, staging, and follow-up, including the essential role of contraception.

Series Learning Outcomes

Upon completing this Series, you should be able to:

- **SLO 4.1:** describe the classification and pathophysiology of hydatidiform mole,
- **SLO 4.2:** describe the clinical presentation and diagnosis of hydatidiform mole,
- **SLO 4.3:** describe the management of hydatidiform mole,
- **SLO 4.4:** describe invasive mole and choriocarcinoma,
- **SLO 4.5:** describe placental site trophoblastic tumour and epithelioid trophoblastic tumour,
- **SLO 4.6:** describe the role of serum beta-hCG and the staging of gestational trophoblastic neoplasia, and
- **SLO 4.7:** describe the treatment and follow-up of gestational trophoblastic neoplasia, including contraception.

4.1 Hydatidiform Mole

4.1.1 Classification and pathophysiology of hydatidiform mole

Hydatidiform mole is classified as complete (arising from fertilisation of an empty ovum, with paternal chromosomes duplicated and no genuine foetal tissue present, entirely androgenetic in origin) or partial (arising from fertilisation of a normal ovum by two sperm, or one sperm with subsequent chromosomal duplication, resulting in a triploid conceptus with some, though genuinely abnormal, foetal tissue present alongside the molar change).

Both types result from abnormal fertilisation producing excessive paternal genetic material relative to maternal genetic material, driving disorganised, excessive trophoblastic proliferation and characteristic hydropic swelling of the chorionic villi, with complete mole carrying a substantially higher risk of subsequent malignant transformation to gestational trophoblastic neoplasia than partial mole, a distinction of considerable practical importance for counselling and subsequent surveillance.

Fill in the blank: Complete hydatidiform mole is entirely _____ in origin, arising from fertilisation of an empty ovum. Partial hydatidiform mole results in a _____ conceptus with some abnormal foetal tissue present.

4.1.2 Clinical presentation and diagnosis of hydatidiform mole

Hydatidiform mole classically presents with vaginal bleeding in early pregnancy, often accompanied by a uterus that is larger than expected for gestational age, hyperemesis gravidarum more severe than typical, and, in some cases, early-onset pre-eclampsia or hyperthyroidism, the latter two reflecting the substantially elevated beta-hCG levels characteristic of molar pregnancy, given the structural similarity between hCG and thyroid-stimulating hormone.

Diagnosis is suggested by a characteristic 'snowstorm' appearance on ultrasound, reflecting the swollen, hydropic chorionic villi, together with a markedly elevated serum beta-hCG level disproportionate to the apparent gestational age, though definitive diagnosis ultimately requires histological confirmation of the products of conception obtained at evacuation.

Fill in the blank: Hydatidiform mole is associated with early-onset pre-eclampsia or hyperthyroidism, reflecting substantially elevated _____ levels. Diagnosis is suggested by a characteristic 'snowstorm' appearance on _____.

4.1.3 Management of hydatidiform mole

Suction evacuation of the uterus under ultrasound guidance is the treatment of choice for hydatidiform mole, performed promptly once the diagnosis is confirmed or strongly suspected, with careful attention to minimising the risk of uterine perforation given the potentially friable, abnormal nature of molar tissue, and anti-D prophylaxis given to rhesus-negative women following evacuation as for any other pregnancy loss.

Following evacuation structured, sustained follow-up with serial serum beta-hCG monitoring is essential to detect the development of persistent or malignant gestational trophoblastic disease at the earliest possible stage, with the woman advised to avoid pregnancy during this specific monitoring period, given that a subsequent pregnancy would otherwise make interpretation of ongoing beta-hCG trends genuinely impossible.

Fill in the blank: Suction evacuation of the uterus is the treatment of choice for hydatidiform mole, with careful attention to minimising the risk of uterine _____. Following evacuation, the woman is advised to avoid _____ during the beta-hCG monitoring period.

Feature	Complete Mole	Partial Mole
Chromosomal Origin	Diploid (usually 46,XX from paternal duplication; no maternal contribution)	Triploid (69,XXY or 69,XXX; two paternal sets + one maternal set)
Foetal Tissue	No foetal tissue present	Some foetal tissue may be present, often abnormal
Malignant Transformation Risk	Higher risk (10–20% progress to persistent trophoblastic disease; risk of choriocarcinoma)	Lower risk (<5% progress to persistent disease; rare choriocarcinoma)

Table 4.1: Comparison of complete and partial hydatidiform mole.

Pilot questions 4.1

- Distinguish complete from partial hydatidiform mole by chromosomal origin. (Linked to SLO 4.1)
- Explain why complete mole carries a higher risk of malignant transformation than partial mole. (Linked to SLO 4.1)
- Describe the clinical presentation of hydatidiform mole. (Linked to SLO 4.2)
- Describe the diagnostic findings suggestive of hydatidiform mole. (Linked to SLO 4.2)
- Describe the management of hydatidiform mole, including follow-up. (Linked to SLO 4.3)

4.2 Gestational Trophoblastic Neoplasia

4.2.1 Invasive mole

Invasive mole describes molar tissue that has invaded into the myometrium, most commonly diagnosed following evacuation of a hydatidiform mole when serum beta-hCG levels plateau or rise rather than progressively declining as expected, representing the most common form of gestational trophoblastic neoplasia and typically responding well to chemotherapy without requiring hysterectomy in the great majority of cases.

Diagnosis of invasive mole is generally made on the basis of the characteristic beta-hCG plateau or rise pattern following evacuation, together with imaging evidence of myometrial invasion, rather than requiring histological confirmation in every case, given the genuine, recognised risks associated with obtaining a further tissue sample from an already vascular, potentially heavily bleeding uterus.

Fill in the blank: Invasive mole is most commonly diagnosed when serum beta-hCG levels plateau or rise rather than progressively _____ following evacuation. Diagnosis of invasive mole is generally made without requiring histological confirmation in every _____.

4.2.2 Choriocarcinoma

Choriocarcinoma is a highly malignant tumour of trophoblastic tissue, arising in roughly equal proportion following a molar pregnancy, a normal pregnancy, or a miscarriage or ectopic pregnancy, characterised by early, aggressive haematogenous spread, most commonly to the lungs, but also to the liver, brain, and other distant sites, making prompt recognition and treatment genuinely essential.

Despite its aggressive behaviour choriocarcinoma is, remarkably, among the most chemosensitive of all human malignancies, with even extensive metastatic disease frequently achieving genuine cure with appropriately selected chemotherapy, reflecting the same underlying biological principle of trophoblastic chemosensitivity that makes gestational trophoblastic neoplasia overall a genuinely notable, encouraging exception to the generally more guarded prognosis associated with metastatic malignancy elsewhere in oncology.

Fill in the blank: Choriocarcinoma is characterised by early, aggressive haematogenous spread, most commonly to the _____. Choriocarcinoma is among the most chemo_____ of all human malignancies, even with extensive metastatic disease.

4.2.3 Placental site trophoblastic tumour and epithelioid trophoblastic tumour

Placental site trophoblastic tumour is a rare form of gestational trophoblastic neoplasia arising from intermediate trophoblast at the placental implantation site, characterised by relatively modest beta-hCG elevation compared with other forms of gestational trophoblastic neoplasia, and, importantly, relative resistance to standard chemotherapy regimens, meaning surgical hysterectomy often represents the primary, most effective treatment for localised disease.

Epithelioid trophoblastic tumour is an even rarer variant, similarly arising from intermediate trophoblast, sharing the relative chemoresistance of placental site trophoblastic tumour, and can present many years after the antecedent pregnancy, occasionally causing genuine diagnostic difficulty when the connection to a remote pregnancy is not immediately apparent or considered.

Fill in the blank: Placental site trophoblastic tumour arises from intermediate trophoblast at the placental _____ site. Both placental site and epithelioid trophoblastic tumours show relative resistance to standard _____ regimens.

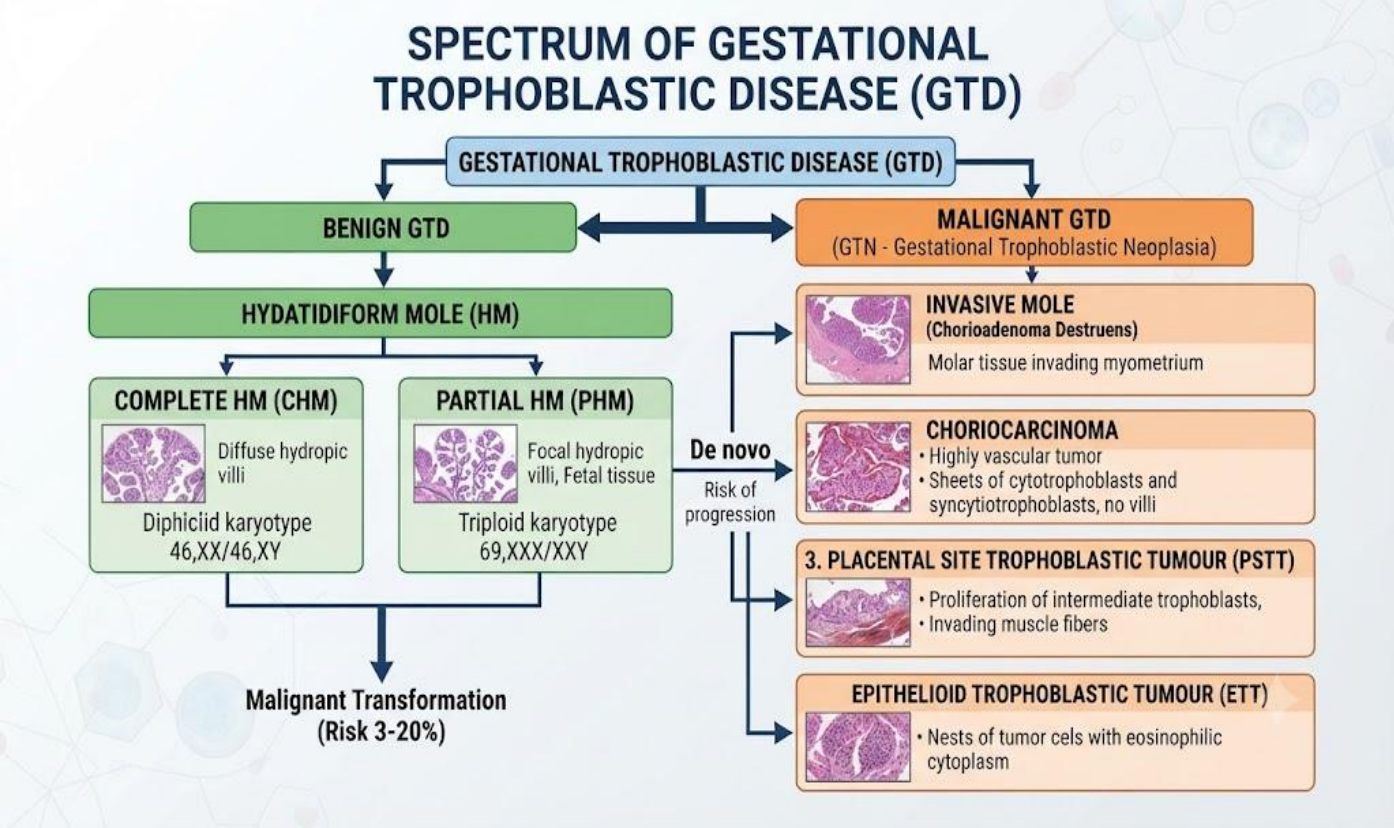

Figure 4.2: The spectrum of gestational trophoblastic disease.

Pilot questions 4.2

1. Describe invasive mole and how it is typically diagnosed. (Linked to SLO 4.4)
2. Describe choriocarcinoma and its pattern of spread. (Linked to SLO 4.4)
3. Explain why choriocarcinoma is considered a notable exception in oncology despite its aggressive behaviour. (Linked to SLO 4.4)
4. Describe placental site trophoblastic tumour and its treatment implications. (Linked to SLO 4.5)
5. Describe epithelioid trophoblastic tumour and the diagnostic challenge it can present. (Linked to SLO 4.5)

4.3 Diagnosis, Staging, and Follow-up

4.3.1 Role of serum beta-hCG in diagnosis and monitoring

Serum beta-hCG is a genuinely central biomarker throughout the entire spectrum of gestational trophoblastic disease, used both in the initial diagnosis of hydatidiform mole and, critically, in structured serial monitoring following evacuation to detect the development of persistent or malignant disease, with a specifically defined pattern of plateau or rise in beta-hCG over successive measurements, rather than a single elevated value, diagnostic of gestational trophoblastic neoplasia requiring treatment.

Beyond diagnosis serum beta-hCG also serves as a genuinely reliable tumour marker for monitoring response to treatment once chemotherapy has been commenced, with a satisfactory, expected decline in beta-hCG confirming adequate treatment response, and a failure to decline as expected prompting reconsideration of the treatment regimen, reflecting the unusually close, reliable correlation between tumour burden and this specific biomarker in gestational trophoblastic disease.

Fill in the blank: A specifically defined pattern of plateau or rise in beta-hCG over successive measurements, rather than a single value, is diagnostic of gestational trophoblastic _____ requiring treatment. Serum beta-hCG serves as a reliable tumour marker for monitoring _____ to treatment.

4.3.2 Staging and risk scoring of gestational trophoblastic neoplasia

Gestational trophoblastic neoplasia is staged using the FIGO anatomical staging system, ranging from stage I (confined to the uterus) through stage II (extending to other genital structures) and stage III (pulmonary metastasis) to stage IV (distant metastasis beyond the lungs), combined with a modified WHO prognostic scoring system incorporating factors such as age, antecedent pregnancy type, interval since that pregnancy, pre-treatment beta-hCG level, tumour size, site and number of metastases, and any previous failed chemotherapy.

This combined staging and scoring system categorises women as low-risk or high-risk, directly guiding the choice between single-agent chemotherapy (generally sufficient for low-risk disease) and multi-agent combination chemotherapy (required for high-risk disease), reflecting a genuinely sophisticated, evidence-based approach to risk-stratified treatment selection that has contributed substantially to the excellent overall cure rates achieved in gestational trophoblastic neoplasia.

Fill in the blank: Gestational trophoblastic neoplasia staging is combined with a modified WHO prognostic scoring system to categorise women as low-risk or _____-risk. Low-risk disease is generally treated with single-agent chemotherapy, while high-risk disease requires _____-agent combination chemotherapy.

4.3.3 Treatment and follow-up, including contraception

Chemotherapy for gestational trophoblastic neoplasia, whether single-agent (typically methotrexate) for low-risk disease or multi-agent combination regimens for high-risk disease, achieves genuinely excellent overall cure rates given the characteristic chemosensitivity of

trophoblastic tissue, with treatment continued until beta-hCG has normalised and then for a further period beyond normalisation to minimise the risk of relapse.

Contraception during and following treatment for gestational trophoblastic disease is genuinely essential, both to avoid the confounding effect a subsequent pregnancy would have on beta-hCG monitoring during the active surveillance period, and, during active chemotherapy specifically, to avoid the teratogenic risk of the chemotherapeutic agents themselves, with reliable contraception, generally excluding an intrauterine device given the theoretical risk of uterine perforation in a uterus recently affected by trophoblastic disease, recommended throughout this specific period.

Fill in the blank: Chemotherapy for low-risk gestational trophoblastic neoplasia typically uses single-agent _____. Contraception during treatment generally excludes an intrauterine device given the theoretical risk of uterine _____.

Category	Details
FIGO Stages	Stage I: confined to uterus. Stage II: extends to genital structures (ovary, vagina, broad ligament). Stage III: lung metastases. Stage IV: other distant metastases (e.g., liver, brain).
Risk Factors (WHO Scoring)	Age >40, antecedent pregnancy type (mole vs term), interval >4 months from pregnancy, high pre-treatment hCG, large tumour size, metastases (number, site), prior chemotherapy. Score ≥7 = high risk.
Treatment by Risk Category	Low-risk (score ≤6): single-agent chemotherapy (methotrexate or actinomycin D). High-risk (score ≥7): multi-agent chemotherapy (EMA-CO regimen). Resistant/relapsed disease: salvage chemotherapy, surgery, or radiotherapy.
Supportive Principles	Close hCG monitoring until normal for 6–12 months; contraception during follow-up; multidisciplinary care.

Box 4.3: Staging, risk scoring, and treatment of gestational trophoblastic neoplasia.

Pilot questions 4.3

1. Describe the role of serum beta-hCG in diagnosing gestational trophoblastic neoplasia. (Linked to SLO 4.6)
2. Describe the FIGO staging system for gestational trophoblastic neoplasia. (Linked to SLO 4.6)

3. Describe the factors included in the modified WHO prognostic scoring system. (Linked to SLO 4.6)
4. Describe the treatment approach for low-risk versus high-risk gestational trophoblastic neoplasia. (Linked to SLO 4.7)
5. Explain why reliable contraception is essential during and after treatment for gestational trophoblastic disease. (Linked to SLO 4.7)

Series Summary

This Series has covered hydatidiform mole, its classification, presentation, diagnosis, and management, followed by gestational trophoblastic neoplasia, including invasive mole, choriocarcinoma, and the rarer placental site and epithelioid trophoblastic tumours. It concluded with the diagnosis, staging, treatment, and follow-up of this disease spectrum, including the essential role of contraception.

You should now be able to describe the classification and management of hydatidiform mole, describe invasive mole and choriocarcinoma, describe placental site and epithelioid trophoblastic tumours, describe the role of beta-hCG and staging in gestational trophoblastic neoplasia, and describe its treatment and follow-up (Linked to SLOs 4.1 to 4.7).

Glossary of Terms

1. **Choriocarcinoma:** a highly malignant, chemosensitive tumour of trophoblastic tissue with a propensity for early haematogenous spread.
2. **Complete hydatidiform mole:** a molar pregnancy entirely androgenetic in origin, arising from fertilisation of an empty ovum, with no true foetal tissue.
3. **Epithelioid trophoblastic tumour:** a rare, chemoresistant form of gestational trophoblastic neoplasia arising from intermediate trophoblast.
4. **Gestational trophoblastic neoplasia (GTN):** the malignant spectrum of gestational trophoblastic disease, including invasive mole, choriocarcinoma, and rarer variants.
5. **Hydatidiform mole:** an abnormal pregnancy characterised by disorganised trophoblastic proliferation, classified as complete or partial.

6. **Invasive mole:** molar tissue that has invaded the myometrium, the most common form of gestational trophoblastic neoplasia.
7. **Partial hydatidiform mole:** a triploid molar pregnancy with some abnormal foetal tissue present, generally carrying lower malignant potential than complete mole.
8. **Placental site trophoblastic tumour:** a rare, relatively chemoresistant form of gestational trophoblastic neoplasia arising at the placental implantation site.
9. **Serum beta-hCG:** the central biomarker used in diagnosing, staging, and monitoring treatment response in gestational trophoblastic disease.
10. **Suction evacuation:** the treatment of choice for hydatidiform mole, removing molar tissue from the uterine cavity.
11. **FIGO anatomical staging:** the staging system for gestational trophoblastic neoplasia, from stage I confined to the uterus to stage IV with distant metastasis.
12. **WHO prognostic scoring system:** a modified scoring system combining multiple factors to categorise gestational trophoblastic neoplasia as low- or high-risk.

Concept Check Questions [Series 4]

Objective questions

1. Complete hydatidiform mole is entirely _____ in origin, arising from fertilisation of an empty ovum.
2. Diagnosis of hydatidiform mole is suggested by a characteristic 'snowstorm' appearance on _____.
3. Choriocarcinoma is characterised by early, aggressive haematogenous spread, most commonly to the _____.
4. Placental site trophoblastic tumour arises from intermediate trophoblast at the placental _____ site.
5. Low-risk gestational trophoblastic neoplasia is generally treated with single-agent _____.

Short-answer questions

- Explain why complete mole carries a higher risk of malignant transformation than partial mole. (Linked to SLO 4.1)
- Describe the management of hydatidiform mole, including follow-up. (Linked to SLO 4.3)
- Explain why choriocarcinoma is considered a notable exception in oncology despite its aggressive behaviour. (Linked to SLO 4.4)
- Describe placental site trophoblastic tumour and its treatment implications. (Linked to SLO 4.5)
- Explain why reliable contraception is essential during and after treatment for gestational trophoblastic disease. (Linked to SLO 4.7)

Long-answer questions

1. Describe the classification, pathophysiology, presentation, diagnosis, and management of hydatidiform mole. (Linked to SLO 4.1, SLO 4.2, SLO 4.3)
2. Describe invasive mole and choriocarcinoma, including their diagnosis and behaviour. (Linked to SLO 4.4)
3. Describe placental site trophoblastic tumour and epithelioid trophoblastic tumour. (Linked to SLO 4.5)
4. Describe the role of serum beta-hCG and the staging system used in gestational trophoblastic neoplasia. (Linked to SLO 4.6)
5. Describe the treatment and follow-up of gestational trophoblastic neoplasia, including the role of contraception. (Linked to SLO 4.7)

Answers to Concept Check Questions [Series 4]

Objective questions

6. Androgenetic.
7. Ultrasound.
8. Lungs.

9. Implantation.
10. Methotrexate.

Short-answer questions

11. Complete mole is entirely androgenetic with excessive paternal genetic material, driving greater trophoblastic proliferation than partial mole.
12. Suction evacuation followed by structured serial beta-hCG monitoring to detect persistent or malignant disease, avoiding pregnancy during surveillance.
13. Despite its aggressive spread, choriocarcinoma is among the most chemosensitive malignancies, with even metastatic disease often curable.
14. It shows relative resistance to standard chemotherapy, making surgical hysterectomy the primary treatment for localised disease.
15. It avoids confounding beta-hCG monitoring and, during chemotherapy, avoids teratogenic risk to a potential pregnancy.

Long-answer questions

16. **Basic response:** Hydatidiform mole is classified as complete or partial, presenting with bleeding and an enlarged uterus, managed by suction evacuation and beta-hCG surveillance.

Value-added response: Complete mole carries higher malignant potential than partial mole, an important distinction guiding counselling and follow-up intensity.

17. **Basic response:** Invasive mole is diagnosed by a beta-hCG plateau or rise after evacuation, while choriocarcinoma spreads early and aggressively but responds excellently to chemotherapy.

Value-added response: Choriocarcinoma's chemosensitivity makes it a notable exception to the generally guarded prognosis of metastatic malignancy elsewhere in oncology.

18. **Basic response:** Placental site and epithelioid trophoblastic tumours are rare, relatively chemoresistant, and often require surgical treatment for localised disease.

Value-added response: Epithelioid trophoblastic tumour can present many years after the antecedent pregnancy, occasionally causing diagnostic difficulty.

19. **Basic response:** Beta-hCG diagnoses and monitors gestational trophoblastic neoplasia, with FIGO staging and WHO scoring together guiding risk-stratified treatment.

Value-added response: This combined system has contributed substantially to the excellent overall cure rates achieved in gestational trophoblastic neoplasia.

20. **Basic response:** Treatment uses single-agent or multi-agent chemotherapy according to risk category, continued beyond beta-hCG normalisation to minimise relapse.

Value-added response: Reliable contraception, generally excluding an intrauterine device, is essential throughout treatment and surveillance.

Answers to Pilot Questions [Series 4]

Part 4.1

11. Complete mole is entirely androgenetic from an empty ovum; partial mole is triploid with some abnormal foetal tissue present.
12. Complete mole has excessive paternal genetic material driving greater trophoblastic proliferation than partial mole.
13. Vaginal bleeding, a uterus larger than expected, severe hyperemesis, and sometimes early pre-eclampsia or hyperthyroidism.
14. A 'snowstorm' appearance on ultrasound and a markedly elevated beta-hCG disproportionate to gestational age.
15. Suction evacuation, with structured serial beta-hCG monitoring and avoidance of pregnancy during surveillance.

Part 4.2

1. Molar tissue invading the myometrium, typically diagnosed by a beta-hCG plateau or rise after evacuation.

2. A highly malignant tumour with early haematogenous spread, most commonly to the lungs.
3. Despite aggressive spread, it is among the most chemosensitive malignancies, often curable even when metastatic.
4. A rare tumour arising at the placental implantation site, relatively chemoresistant, often requiring hysterectomy.
5. An even rarer variant that can present years after the antecedent pregnancy, occasionally causing diagnostic difficulty.

Part 4.3

6. It diagnoses molar pregnancy and, through a plateau or rise pattern, identifies gestational trophoblastic neoplasia after evacuation.
7. Stage I (confined to uterus), stage II (other genital structures), stage III (pulmonary metastasis), and stage IV (distant metastasis).
8. Age, antecedent pregnancy type, interval since pregnancy, pre-treatment beta-hCG, tumour size, metastatic site and number, and prior failed chemotherapy.
9. Single-agent chemotherapy for low-risk disease, multi-agent combination chemotherapy for high-risk disease.
10. It avoids confounding beta-hCG monitoring from a new pregnancy and avoids teratogenic risk during chemotherapy.

References and Attributions [Series 4]

Textual References

11. Hoffman, B. L., Schorge, J. O., Halvorson, L. M. et al. (2020). Williams Gynecology (4th ed.). McGraw Hill.
12. International Federation of Gynecology and Obstetrics (2021). FIGO Cancer Report. FIGO.
13. Royal College of Obstetricians and Gynaecologists (2020). Green-top Guideline No. 38: Gestational Trophoblastic Disease. RCOG Press.

14. National Comprehensive Cancer Network (2023). NCCN Clinical Practice Guidelines in Oncology: Gestational Trophoblastic Neoplasia. NCCN.

Figures, Plates, Tables, and Boxes

1. Table 4.1: Comparison of complete and partial hydatidiform mole. AI-generated using the prompt: "Create a clean reference table titled Complete versus Partial Hydatidiform Mole, comparing chromosomal origin, foetal tissue, and malignant transformation risk. Simple clinical reference table style with outside border."
2. Figure 4.2: The spectrum of gestational trophoblastic disease. AI-generated using the prompt: "Create a professional medical diagram titled Spectrum of Gestational Trophoblastic Disease, showing the relationship between molar disease, invasive mole, choriocarcinoma, and rarer tumour types. Clean clinical educational diagram style."
3. Box 4.3: Staging, risk scoring, and treatment of gestational trophoblastic neoplasia. AI-generated using the prompt: "Create a simple single-column reference box with an outside border titled GTN Staging and Risk-Based Treatment, listing FIGO stages, risk factors, and treatment by risk category. Clinical reference box style."

Series 5: Oncologic Therapies in Gynaecology

- **Part 5.1: Principles of Chemotherapy in Gynaecological Cancer**
    - Sub Part 5.1.1: Mechanism and classes of chemotherapeutic agents
    - Sub Part 5.1.2: Chemotherapy regimens by cancer type
    - Sub Part 5.1.3: Side effects and toxicity of chemotherapy
- **Part 5.2: Principles of Radiotherapy in Gynaecological Cancer**
    - Sub Part 5.2.1: Mechanism and types of radiotherapy
    - Sub Part 5.2.2: Radiotherapy regimens by cancer type
    - Sub Part 5.2.3: Side effects and toxicity of radiotherapy
- **Part 5.3: Integrating Oncologic Therapies and Course Synthesis**
    - Sub Part 5.3.1: Combined modality treatment and multidisciplinary care
    - Sub Part 5.3.2: Supportive and survivorship care
    - Sub Part 5.3.3: Course synthesis: from lesion recognition to oncologic treatment

Introduction

In the last Series, we explored gestational trophoblastic diseases. We conclude this course, and this journey through Gynaecological Oncology, by turning to the chemotherapy and radiotherapy that so often complete the treatment of the cancers covered throughout every preceding Series: vulval, cervical, uterine, ovarian, and gestational trophoblastic disease alike. This final Series brings together the pharmacological and physical principles of these two central oncologic therapies, and reflects on the genuinely multidisciplinary, compassionate practice of gynaecological oncology as a whole.

The aim of this Series is to equip you with a thorough understanding of chemotherapy and radiotherapy in gynaecological cancer, and the principles of multidisciplinary, supportive, and survivorship care.

We shall commence this Series by examining the principles of chemotherapy in gynaecological cancer, including its mechanisms, regimens, and side effects. Next, we will consider the principles of radiotherapy, including its mechanisms, regimens, and side effects. Finally, we will

conclude by examining combined modality treatment, multidisciplinary care, and supportive and survivorship care, bringing this course to a close.

Series Learning Outcomes

Upon completing this Series, you should be able to:

- **SLO 5.1:** describe the mechanism and classes of chemotherapeutic agents used in gynaecological cancer,
- **SLO 5.2:** describe chemotherapy regimens used by gynaecological cancer type,
- **SLO 5.3:** describe the side effects and toxicity of chemotherapy,
- **SLO 5.4:** describe the mechanism and types of radiotherapy used in gynaecological cancer,
- **SLO 5.5:** describe radiotherapy regimens and side effects by cancer type,
- **SLO 5.6:** describe the principles of combined modality treatment and multidisciplinary care, and
- **SLO 5.7:** describe the principles of supportive and survivorship care in gynaecological oncology.

5.1 Principles of Chemotherapy in Gynaecological Cancer

5.1.1 Mechanism and classes of chemotherapeutic agents

Chemotherapeutic agents used in gynaecological cancer act principally by disrupting cell division and inducing cell death in rapidly proliferating tumour cells, with platinum agents (such as cisplatin and carboplatin, forming DNA cross-links that prevent replication) representing the cornerstone of treatment across ovarian, cervical, and endometrial cancer, generally combined with a taxane (such as paclitaxel, disrupting microtubule function and preventing normal cell division) in many standard regimens.

Other agent classes relevant to gynaecological oncology include alkylating agents, topoisomerase inhibitors, and, increasingly, targeted biological agents such as bevacizumab (an anti-angiogenic monoclonal antibody inhibiting new blood vessel formation to the tumour) and PARP inhibitors (exploiting a specific DNA repair vulnerability, particularly effective in ovarian cancer with a BRCA mutation or other homologous recombination deficiency), reflecting the genuinely rapid evolution of gynaecological cancer treatment beyond conventional cytotoxic chemotherapy alone.

Fill in the blank: Platinum agents form DNA cross-links that prevent _____, representing the cornerstone of treatment across ovarian, cervical, and endometrial cancer. PARP inhibitors exploit a specific DNA repair vulnerability, particularly effective in ovarian cancer with a _____ mutation.

5.1.2 Chemotherapy regimens by cancer type

In ovarian cancer combination platinum and taxane chemotherapy is standard, given either after primary cytoreductive surgery or, in selected cases of extensive disease, as neoadjuvant treatment before interval surgery, with maintenance therapy, including PARP inhibitors in appropriately selected women, increasingly used following completion of initial chemotherapy to extend the duration of disease remission.

In cervical cancer concurrent platinum-based chemotherapy alongside radiotherapy is standard for locally advanced disease, acting as a radiosensitiser to enhance the effectiveness of radiotherapy, while in endometrial cancer, chemotherapy, generally combining a platinum agent and a taxane, is used as adjuvant treatment for higher-risk disease identified at surgical staging, or for advanced or recurrent disease where surgery alone would be insufficient.

Fill in the blank: In cervical cancer, concurrent platinum-based chemotherapy acts as a _____ to enhance the effectiveness of radiotherapy. In endometrial cancer, chemotherapy is used as adjuvant treatment for higher-_____ disease identified at surgical staging.

5.1.3 Side effects and toxicity of chemotherapy

Common side effects of chemotherapy include nausea and vomiting (generally well controlled with modern antiemetic regimens), myelosuppression (increasing the risk of infection, anaemia, and bleeding), alopecia, and peripheral neuropathy, particularly associated with taxane and platinum agents, each requiring specific, proactive monitoring and supportive management throughout the course of treatment.

Neutropenic sepsis (fever occurring in the context of a low neutrophil count following chemotherapy) is a genuine oncological emergency requiring immediate assessment and prompt initiation of broad-spectrum antibiotics, with every woman receiving chemotherapy specifically counselled beforehand about this risk and given clear, explicit instructions on when and how to seek urgent medical attention should fever develop during the vulnerable period following treatment.

Fill in the blank: Peripheral neuropathy is a common side effect particularly associated with taxane and _____ agents. Neutropenic sepsis is a genuine oncological _____ requiring immediate assessment and prompt antibiotics.

Class	Mechanism	Example Agents
Alkylating Agents	Cross-link DNA strands → inhibit replication	Cyclophosphamide, Ifosfamide

Class	Mechanism	Example Agents
Platinum Compounds	DNA cross-linking → apoptosis	Cisplatin, Carboplatin
Antimetabolites	Inhibit nucleotide synthesis → block DNA/RNA replication	Methotrexate, 5-Fluorouracil
Topoisomerase Inhibitors	Prevent DNA unwinding → strand breaks	Doxorubicin (Topo II), Topotecan (Topo I)
Taxanes	Stabilize microtubules → inhibit mitosis	Paclitaxel, Docetaxel
Vinca Alkaloids	Prevent microtubule assembly → block mitosis	Vincristine, Vinblastine
Targeted Therapy	Inhibit specific molecular pathways	Bevacizumab (anti-VEGF), PARP inhibitors (Olaparib)

Table 5.1: Chemotherapeutic agent classes used in gynaecological cancer.

Pilot questions 5.1

- Describe the mechanism of platinum agents and taxanes. (Linked to SLO 5.1)
- Describe the mechanism of bevacizumab and PARP inhibitors. (Linked to SLO 5.1)
- Describe the chemotherapy regimen used in ovarian cancer. (Linked to SLO 5.2)
- Describe the role of chemotherapy in cervical and endometrial cancer. (Linked to SLO 5.2)
- Describe neutropenic sepsis and its management. (Linked to SLO 5.3)

5.2 Principles of Radiotherapy in Gynaecological Cancer

5.2.1 Mechanism and types of radiotherapy

Radiotherapy uses ionising radiation to damage tumour cell DNA, causing cell death or preventing further cell division, delivered either as external beam radiotherapy (radiation delivered from an external source directed at the pelvis or affected region) or brachytherapy (radioactive sources placed directly within or close to the tumour, delivering a high, precisely localised dose while relatively sparing surrounding normal tissue).

Brachytherapy is of particular importance in cervical cancer treatment, typically delivered following a course of external beam radiotherapy, allowing a further, highly localised radiation

boost to the cervix and surrounding tissue that could not be safely delivered by external beam radiotherapy alone without unacceptable toxicity to nearby normal structures, including the bladder and rectum.

Fill in the blank: Radiotherapy uses ionising radiation to damage tumour cell _____, causing cell death or preventing further division. Brachytherapy delivers a high, precisely localised dose while relatively sparing surrounding _____ tissue.

5.2.2 Radiotherapy regimens by cancer type

In cervical cancer radiotherapy, generally combined with concurrent platinum-based chemotherapy, is the standard treatment for locally advanced disease (stage IIB to IVA), comprising external beam radiotherapy to the pelvis followed by brachytherapy, with the overall treatment course carefully planned and sequenced to minimise unnecessary treatment gaps, given evidence that prolonged overall treatment time can meaningfully reduce treatment effectiveness.

In endometrial cancer adjuvant radiotherapy, either external beam or vaginal vault brachytherapy alone for lower-risk disease, is used following surgery for women with identified pathological risk factors for recurrence, reducing the risk of local, particularly vaginal vault, recurrence, while radiotherapy also has an important, well-established role in the palliative management of symptomatic pelvic recurrence or metastatic disease across gynaecological cancer types more broadly.

Fill in the blank: Cervical cancer radiotherapy comprises external beam radiotherapy to the pelvis followed by _____. Radiotherapy has an important, well-established role in the _____ management of symptomatic pelvic recurrence or metastatic disease.

5.2.3 Side effects and toxicity of radiotherapy

Acute side effects of pelvic radiotherapy include fatigue, skin reaction within the treated field, and gastrointestinal symptoms such as diarrhoea and abdominal cramping, generally developing during the course of treatment and resolving over subsequent weeks following its completion, managed with appropriate supportive measures including dietary advice and antidiarrhoeal medication where needed.

Longer-term, late effects of pelvic radiotherapy can include vaginal stenosis and dryness (affecting sexual function and requiring proactive counselling and, where appropriate, use of vaginal dilators), bowel and bladder dysfunction, and, rarely, secondary malignancy arising many years after treatment, each requiring genuine, honest discussion with the woman before treatment begins, as part of properly informed consent for radiotherapy as a treatment modality.

Fill in the blank: Acute side effects of pelvic radiotherapy generally resolve over subsequent weeks following the completion of _____. Late effects of pelvic radiotherapy can include vaginal stenosis, requiring proactive counselling and use of vaginal _____.

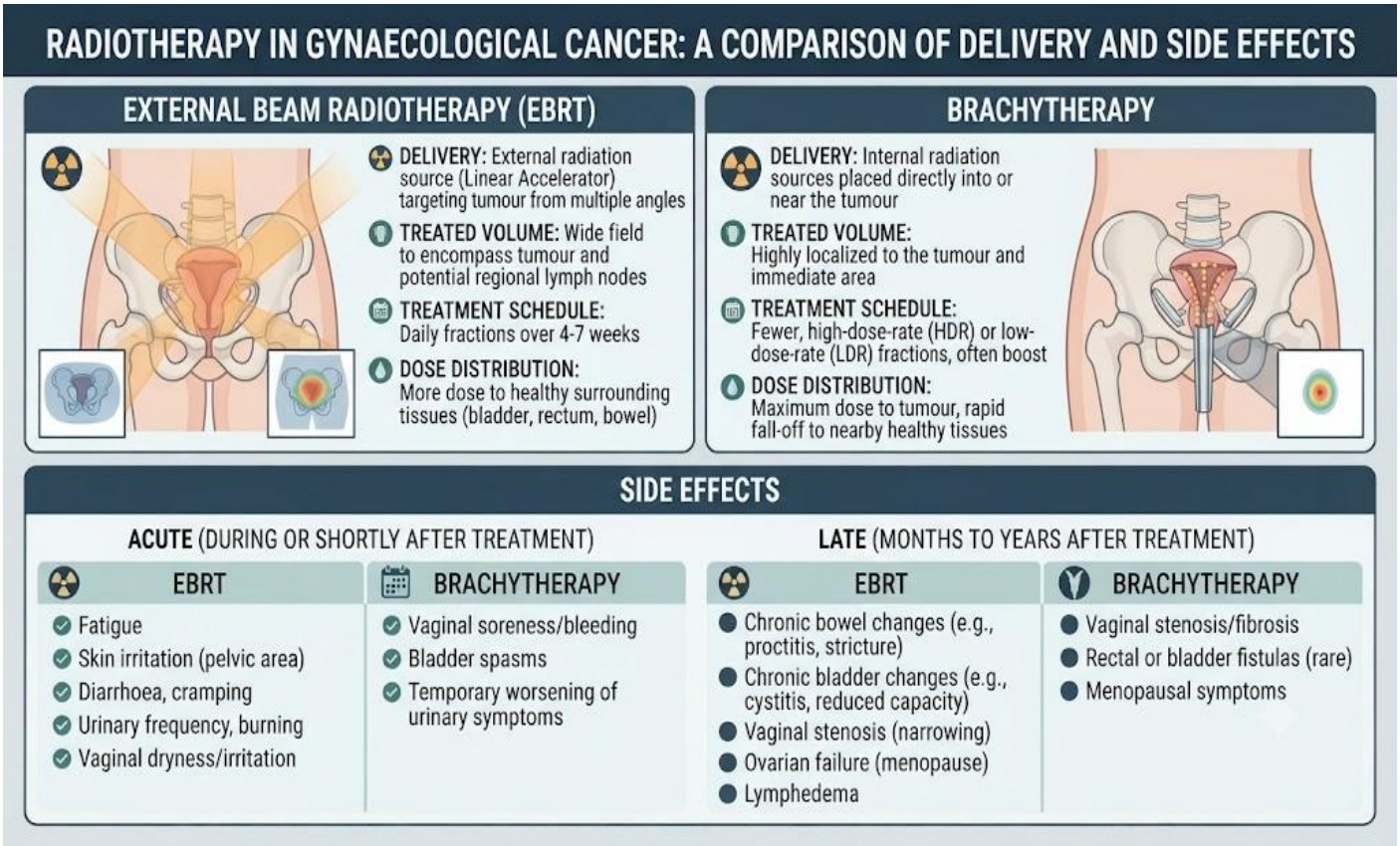

Figure 5.2: External beam radiotherapy versus brachytherapy, and acute versus late side effects.

Pilot questions 5.2

1. Describe the mechanism of radiotherapy and distinguish external beam radiotherapy from brachytherapy. (Linked to SLO 5.4)
2. Explain the particular importance of brachytherapy in cervical cancer treatment. (Linked to SLO 5.4)
3. Describe the radiotherapy regimen used for locally advanced cervical cancer. (Linked to SLO 5.5)
4. Describe the role of radiotherapy in endometrial cancer and in palliative care. (Linked to SLO 5.5)
5. Describe the acute and late side effects of pelvic radiotherapy. (Linked to SLO 5.5)

5.3 Integrating Oncologic Therapies and Course Synthesis

5.3.1 Combined modality treatment and multidisciplinary care

Combined modality treatment (surgery, chemotherapy, and radiotherapy used together or in sequence) reflects the genuinely complex, individualised nature of modern gynaecological cancer management, with the specific combination and sequence of treatments determined through discussion at a multidisciplinary team meeting, bringing together gynaecological oncology surgeons, clinical and medical oncologists, radiologists, pathologists, and specialist nursing staff to agree the optimal, evidence-based treatment plan for each individual woman.

This multidisciplinary approach ensures that treatment decisions genuinely reflect the full breadth of relevant expertise, and that the specific sequence and combination of modalities selected for each woman is based on her individual disease stage, histology, and overall clinical circumstances, rather than a single specialist's isolated perspective, reflecting the genuinely collaborative, team-based nature of contemporary cancer care that runs consistently throughout this entire course.

Fill in the blank: The specific combination and sequence of treatments is determined through discussion at a _____ team meeting. This approach ensures treatment decisions reflect the full breadth of relevant _____ rather than a single specialist's isolated perspective.

5.3.2 Supportive and survivorship care

Supportive care throughout gynaecological cancer treatment addresses symptom management, nutritional support, psychological and emotional wellbeing, and, where relevant, fertility preservation counselling before treatment begins, recognising that effective cancer care genuinely extends well beyond the specific oncologic treatment itself to encompass the woman's overall wellbeing and quality of life throughout her entire treatment journey.

Survivorship care following completion of treatment addresses structured surveillance for recurrence, management of longer-term treatment-related effects including those on sexual function and fertility, and support for the woman's return to normal daily life and activities, an area of gynaecological oncology receiving genuinely increasing recognition and dedicated attention as overall cancer survival rates have continued to improve.

Fill in the blank: Supportive care addresses symptom management, nutritional support, psychological wellbeing, and, where relevant, _____ preservation counselling. Survivorship care addresses structured surveillance for recurrence and management of longer-term treatment-related _____.

5.3.3 Course synthesis: from lesion recognition to oncologic treatment

Across this entire course we have travelled from the anatomy and benign lesions of the vulva and vagina, through cervical disorders and cancer, uterine and ovarian tumours, and gestational trophoblastic disease, to this final Series on the chemotherapy and radiotherapy that so often complete the treatment of these conditions, a deliberate progression reflecting the genuine clinical pathway a woman with gynaecological cancer actually travels, from initial presentation through diagnosis, staging, and, ultimately, treatment.

As you move forward into clinical practice, remember that behind every histological diagnosis, every FIGO stage, and every treatment protocol covered throughout this course stands an individual woman navigating what is often the most frightening experience of her life, and that genuinely excellent gynaecological oncology practice combines the rigorous, evidence-based clinical knowledge this course has built with the same compassion, respect, and clear communication emphasised throughout every other course in this broader curriculum.

Fill in the blank: This course has progressed from vulval and vaginal lesions through cervical, uterine, ovarian, and trophoblastic disease to this final Series on chemotherapy and _____. Genuinely excellent gynaecological oncology practice combines rigorous clinical knowledge with compassion, respect, and clear _____.

Category	Details
Team Members	Gynaecologic oncologist, medical oncologist, radiation oncologist, pathologist, radiologist, oncology nurse, palliative care specialist, psychologist, social worker, physiotherapist, dietitian
Treatment Coordination	Integrated planning of surgery, chemotherapy, radiotherapy; regular tumour board reviews; evidence-based protocols
Supportive Care	Pain and symptom management, nutritional support, psychosocial counselling, fertility preservation, sexual health care
Survivorship Principles	Long-term follow-up, surveillance for recurrence, management of late effects, lifestyle modification, rehabilitation, patient education, community reintegration

Box 5.3: The multidisciplinary team and components of supportive and survivorship care.

Pilot questions 5.3

1. Describe the concept of combined modality treatment in gynaecological cancer. (Linked to SLO 5.6)
2. Describe the composition and value of the multidisciplinary team meeting. (Linked to SLO 5.6)
3. Describe the components of supportive care during gynaecological cancer treatment. (Linked to SLO 5.7)
4. Describe the components of survivorship care following completion of treatment. (Linked to SLO 5.7)
5. Reflect on how clinical knowledge and compassionate communication together underpin excellent gynaecological oncology practice. (Linked to SLO 5.7)

Series Summary

This Series has covered the principles of chemotherapy in gynaecological cancer, including its mechanisms, regimens, and side effects, followed by the principles of radiotherapy, including its mechanisms, regimens, and side effects. It concluded with combined modality treatment, multidisciplinary care, and supportive and survivorship care, bringing this course on Gynaecological Oncology to a close.

You should now be able to describe the mechanism and classes of chemotherapeutic agents, describe chemotherapy regimens by cancer type, describe chemotherapy side effects, describe radiotherapy mechanisms and regimens, describe radiotherapy side effects, describe combined modality and multidisciplinary care, and describe supportive and survivorship care (Linked to SLOs 5.1 to 5.7).

Glossary of Terms

1. **Bevacizumab:** an anti-angiogenic monoclonal antibody inhibiting new blood vessel formation to a tumour.
2. **Brachytherapy:** radiotherapy delivered by radioactive sources placed directly within or close to the tumour.
3. **Chemoradiotherapy:** combined treatment using concurrent chemotherapy and radiotherapy, standard for locally advanced cervical cancer.
4. **External beam radiotherapy:** radiotherapy delivered from an external source directed at the affected region.
5. **Multidisciplinary team meeting:** a structured meeting bringing together relevant specialists to agree an individualised cancer treatment plan.
6. **Myelosuppression:** reduced bone marrow function from chemotherapy, increasing the risk of infection, anaemia, and bleeding.
7. **Neutropenic sepsis:** fever occurring in the context of a low neutrophil count following chemotherapy, a genuine oncological emergency.
8. **PARP inhibitor:** a targeted agent exploiting a DNA repair vulnerability, particularly effective in BRCA-mutated ovarian cancer.
9. **Radiosensitiser:** an agent, such as platinum chemotherapy, that enhances the effectiveness of radiotherapy when given concurrently.
10. **Survivorship care:** structured care following completion of cancer treatment, addressing surveillance and long-term treatment effects.

11. **Vaginal vault brachytherapy:** brachytherapy delivered to the vaginal vault, used as adjuvant treatment following surgery for endometrial cancer.
12. **Taxane:** a chemotherapy class disrupting microtubule function, commonly combined with platinum agents in gynaecological cancer.

Concept Check Questions [Series 5]

Objective questions

1. Platinum agents form DNA cross-links that prevent _____.
2. In cervical cancer, concurrent platinum-based chemotherapy acts as a _____ to enhance radiotherapy effectiveness.
3. Neutropenic sepsis is a genuine oncological _____ requiring immediate assessment and antibiotics.
4. Brachytherapy delivers a high, precisely localised dose while relatively sparing surrounding _____ tissue.
5. The specific combination and sequence of treatments is determined through discussion at a _____ team meeting.

Short-answer questions

- Describe the mechanism of bevacizumab and PARP inhibitors. (Linked to SLO 5.1)
- Describe the role of chemotherapy in cervical and endometrial cancer. (Linked to SLO 5.2)
- Explain the particular importance of brachytherapy in cervical cancer treatment. (Linked to SLO 5.4)
- Describe the acute and late side effects of pelvic radiotherapy. (Linked to SLO 5.5)
- Describe the components of survivorship care following completion of treatment. (Linked to SLO 5.7)

Long-answer questions

1. Describe the mechanism, classes, and side effects of chemotherapy used in gynaecological cancer. (Linked to SLO 5.1, SLO 5.3)
2. Describe chemotherapy regimens used across gynaecological cancer types. (Linked to SLO 5.2)
3. Describe the mechanism, types, regimens, and side effects of radiotherapy in gynaecological cancer. (Linked to SLO 5.4, SLO 5.5)
4. Describe the principles of combined modality treatment and multidisciplinary care. (Linked to SLO 5.6)
5. Describe the principles of supportive and survivorship care in gynaecological oncology. (Linked to SLO 5.7)

Answers to Concept Check Questions [Series 5]

Objective questions

6. Replication.
7. Radiosensitiser.
8. Emergency.
9. Normal.
10. Multidisciplinary.

Short-answer questions

11. Bevacizumab inhibits new blood vessel formation to the tumour; PARP inhibitors exploit a DNA repair vulnerability, effective in BRCA-mutated cancer.
12. Concurrent chemoradiotherapy is standard for locally advanced cervical cancer; chemotherapy is adjuvant treatment in higher-risk endometrial cancer.
13. It allows a highly localised radiation boost that could not be safely delivered by external beam radiotherapy alone without unacceptable toxicity.

14. Acute effects include fatigue, skin reaction, and gastrointestinal symptoms; late effects include vaginal stenosis, and bowel and bladder dysfunction.
15. Structured surveillance for recurrence, management of long-term treatment effects, and support for return to normal daily activities.

Long-answer questions

16. **Basic response:** Chemotherapy in gynaecological cancer principally uses platinum and taxane agents, with newer targeted agents including bevacizumab and PARP inhibitors, and side effects requiring proactive monitoring.

Value-added response: Neutropenic sepsis is a genuine emergency requiring clear patient counselling and prompt antibiotic treatment when it occurs.

17. **Basic response:** Ovarian cancer uses platinum-taxane combination with maintenance therapy; cervical cancer uses concurrent chemoradiotherapy; endometrial cancer uses adjuvant chemotherapy for high-risk disease.

Value-added response: Regimen selection is genuinely individualised according to cancer type, stage, and the woman's overall clinical circumstances.

18. **Basic response:** Radiotherapy uses external beam and brachytherapy, with cervical cancer combining both alongside chemotherapy, and side effects ranging from acute to late.

Value-added response: Late effects such as vaginal stenosis require proactive counselling and management before treatment begins, as part of informed consent.

19. **Basic response:** Combined modality treatment is planned through multidisciplinary team discussion, bringing together relevant specialists for each individual woman.

Value-added response: This collaborative approach reflects the genuinely team-based nature of contemporary gynaecological cancer care.

20. **Basic response:** Supportive care addresses symptom management and wellbeing during treatment, while survivorship care addresses surveillance and long-term effects afterward.

Value-added response: Excellent gynaecological oncology practice combines rigorous clinical knowledge with genuine compassion and clear communication throughout the woman's journey.

Answers to Pilot Questions [Series 5]

Part 5.1

11. Platinum agents form DNA cross-links preventing replication; taxanes disrupt microtubule function preventing cell division.
12. Bevacizumab inhibits new blood vessel formation; PARP inhibitors exploit a DNA repair vulnerability, effective in BRCA-mutated cancer.
13. Combination platinum and taxane chemotherapy, given after primary surgery or as neoadjuvant treatment before interval surgery.
14. Concurrent chemoradiotherapy in locally advanced cervical cancer, and adjuvant or advanced-disease treatment in endometrial cancer.
15. Fever with a low neutrophil count following chemotherapy, a genuine emergency requiring immediate assessment and antibiotics.

Part 5.2

1. External beam radiotherapy is delivered from an external source; brachytherapy places radioactive sources within or close to the tumour.
2. It allows a highly localised radiation boost not safely achievable by external beam radiotherapy alone without unacceptable toxicity.
3. External beam radiotherapy to the pelvis followed by brachytherapy, generally combined with concurrent chemotherapy.
4. Adjuvant radiotherapy reduces local recurrence risk in higher-risk endometrial cancer, and radiotherapy has a well-established palliative role.
5. Acute effects include fatigue, skin reaction, and gastrointestinal symptoms; late effects include vaginal stenosis and bowel or bladder dysfunction.

Part 5.3

6. Surgery, chemotherapy, and radiotherapy used together or in sequence, reflecting the complex, individualised nature of cancer management.

7. Gynaecological oncology surgeons, oncologists, radiologists, pathologists, and specialist nurses, ensuring decisions reflect full relevant expertise.
8. Symptom management, nutritional support, psychological wellbeing, and fertility preservation counselling before treatment begins.
9. Structured surveillance for recurrence, management of long-term treatment effects, and support for return to normal daily activities.
10. Rigorous, evidence-based clinical knowledge combined with genuine compassion, respect, and clear communication throughout the woman's care.

References and Attributions [Series 5]

Textual References

11. Hoffman, B. L., Schorge, J. O., Halvorson, L. M. et al. (2020). Williams Gynecology (4th ed.). McGraw Hill.
12. National Comprehensive Cancer Network (2023). NCCN Clinical Practice Guidelines in Oncology: Ovarian Cancer. NCCN.
13. International Federation of Gynecology and Obstetrics (2021). FIGO Cancer Report. FIGO.
14. Royal College of Radiologists (2019). Radiotherapy Dose Fractionation (3rd ed.). Royal College of Radiologists.

Figures, Plates, Tables, and Boxes

1. Table 5.1: Chemotherapeutic agent classes used in gynaecological cancer. AI-generated using the prompt: "Create a clean reference table titled Chemotherapeutic Agent Classes in Gynaecological Cancer, listing mechanism and example agents. Simple clinical reference table style with outside border."
2. Figure 5.2: External beam radiotherapy versus brachytherapy, and acute versus late side effects. AI-generated using the prompt: "Create a professional medical diagram titled Radiotherapy in Gynaecological Cancer, comparing external beam and brachytherapy delivery with acute and late side effects. Clean clinical educational diagram style."

3. Box 5.3: The multidisciplinary team and components of supportive and survivorship care. AI-generated using the prompt: "Create a simple single-column reference box with an outside border titled Multidisciplinary Care and Survivorship, listing team members and key care components. Clinical reference box style."